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ANIMAL CHEMISTRY

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Chemistry (Animal)

ANIMAL CHEMISTRY

OR

THE RELATIONS OF CHEMISTRY TO PHYSIOLOGY AND PATHOLOGY

A MANUAL for MEDICAL MEN and SCIENTIFIC CHEMISTS

BY

CHARLES THOMAS KINGZETT, F.C.S.

Member of Council of the Institute of Chemistry of Great Britain and Ireland
Author of 'History, Products, and Processes of the Alkali Trade' &c.

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TO THE

REV. E. CAPEL CURE, M.A.

RECTOR OF ST. GEORGE, HANOVER SQUARE

WHOSE KINDNESS AND GOODNESS

ARE AMONG THE AUTHOR'S BRIGHTEST MEMORIES

OF HIS CHILDHOOD

This Work is Inscribed

IN AFFECTION AND GRATITUDE

PREFACE.

FOR FOUR YEARS I was occupied with the practical study of subjects comprehended in the following chapters, and during the whole of that time there were no fluctuations in the success attending the labours in which my services were involved. The field of research was a comparatively new one, and in whatever direction the methods of science were applied, results of no doubtful meaning were obtained. Simultaneously with these discoveries greater fields for research came to view; so quickly, indeed, that at every point the hand failed to keep time with the mind. It was therefore a matter of sincere regret with me that circumstances (which are said to be stronger than men) ultimately necessitated the discontinuance of my connection with work which had given me so much real pleasure.

Pleasure is a different thing to different men. The poet, in contemplating the harmony of nature which he perceives beneath its rugged heterogeneity, and to whom every blossom and every bough shaken with the wind conveys a sense of the beautiful or the wild, finds his greatest pleasure in his own thoughts. So again, the artist gazing upon his handiwork; lost in the wonderwork of his skill, the lines of beauty wrought by his hand, he sees therein the expression of his own fancy, and his cunning is pleasure to him. The scientist knows also his own pleasure. For if the poet, listening to the surge of seas, may live over again an age that is buried, or may be reminded of another sound which was once dear to his heart, so surely the scientist may prolong his intellectual sight into the future with a corresponding emotion.

As the excitation of a memory may hold the hand and the heart spell-bound, so the anticipation of a coming event may be a cause of equal pleasure, and with the scientist such anticipations, composed as they often are half of logical inference and half of intuitive assumption, are not of rare occurrence.

The scientist is a greater philosopher than the sentimentalist, for while the latter pays his addresses to heterogeneous nature as a whole, the former condescends to details, decomposing and reconstructing; and the innate perception of harmony lodged in the brain of the poet, becomes at the hands of the scientist an established law abiding with mathematical exactitude.

Given a line of inductive reasoning based upon experimental data, and its proper pursuit must lead sooner or later, rarely or more often, to discovery. The discovery may be of a substance, of a law, or better still, a generalisation; and the imagination, ever quicker than the hand, traces out the interworkings and connections of the discovery, perpetuating its effect into the future. But the attendant pleasure is reasonable, and may be alluded to without conceit.

It was natural, then, that having experienced so much pleasure, I should be moved with equal regret in resigning the practical study of physiological chemistry; and in order to complete a well-remembered but brief connection with this subject, I determined to attempt a task which should prove of service to scientific men, namely, to collect and systematise, as far as could be, all the trustworthy work on record in relation to Animal Chemistry, so far as it concerns the human body.

The task has proved heavy, because the literature that had to be waded through was so enormous and was scattered broadcast. Moreover, the sifting of the good work from the bad was equally exhaustive. However, I have tried to do my work faithfully and to the best of my ability, and if I have wronged any investigator it has been done unconsciously.

I may explain that it has not been my object to collate every fact which may fairly be included in the subject of physiological chemistry, nor to detail well-known methods of analysis, but rather to present, in as natural an order as possible, all those parts of the subject which, when properly arranged, present something like a system. In doing this, the various methods of research have been particularly described, and even researches published up to date have been included; further, I have endeavoured to comprehend in the scheme of the work, every known subject having a direct relation with the objects of Animal Chemistry.

The proper understanding of the book will depend to a large extent upon the reader's knowledge of chemistry; but this is inevitable; and as pure chemistry is taught to some extent in our medical schools, and so well treated in many excellent text-books, I have not thought it necessary to enter into the subject except in an incidental manner here and there. I have availed myself freely of all existing treatises upon the subject of this work, and have given full references.

In conclusion, I earnestly hope (as I also believe) that scientific chemists will find the volume useful as a guide to them in their researches; and with this thought before me, I have given a category of subjects calling for further investigation at their hands; while for medical men my object has been to present them with a comprehensive account of the most important subject included in their studies and profession.

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PART I.

GENERAL

CHAPTER I.

INTRODUCTORY.

In the village of Vorhout, near Leyden, in 1668, was born the man who in after life founded the science of organic chemistry, properly so called. Learned in medicine, chemistry, and botany, he constituted a type of men who in later days have stood out from the crowd of workers, not only as peculiarly qualified to undertake their self-set tasks in organic chemistry, but also as the most successful of workers, if the amount of success be judged by the weight and importance of the obtained results.

As Professor in the University of Leyden, Hermann Boerhaave made its medical school famous throughout the world. Guided by sound ideas of the nature of life, and devoted to the experimental phases of science, he attracted by his discoveries a crowd of students who afterwards became the leading men of their day.

Beyond the assumption of a 'vital force' and mysterious notions regarding 'vital fluids' which were supposed to exist in animals and plants, the alchemists of Boerhaave's time were without a thought as to the nature and composition of the various matters entering into their substance. It is true that the first observation of plant life was made by the wandering physician, Van Helmont (born 1577), who nourished a small tree from a twig of willow by means, as he thought, of pure water. But the experiment was not understood, and Van Helmont said that the tree was developed out of the matter of the water by the agency of vital force. Indeed, it does not appear from the writings of that time that the constituents of animal substances were viewed as partaking of an ordinary chemical identity. So absorbed were the metaphysicists and alchemists in problems incapable of solution by human efforts; in imaginings outside reason; and so carried away by fanaticism, that to condescend to the study of nature by ordinary observation was a thing of which they had no conception.

It must not be supposed that all the labours since the days of Hippocrates and Aristotle, or even of Galen, the physician, had gone for nothing. Vesalius, Harvey, Malpighi, Grew, and others had slowly but accurately worked at the various organs of the body, and demonstrated many functions in the act of life.

Boerhaave, however, was the first to apply the principles of experimental chemistry to the materials of which these organs were constituted, and to those existing in plants, and by so doing he obtained various extractives, essential oils, camphors, resins, and salts; not merely this, but he also conducted investigations upon milk, blood, and bile, and sought to determine how they conveyed nourishment to the body. His contemporaries in pure chemical science were also working industriously, and out of the multiform discoveries of new elements and compounds, theories and specific laws were constructed and established. Such advances gave to other men the cue whereby they in their turn increased the sum of knowledge of animal chemistry.

Boerhaave not only ascertained the composition of some of the principles obtained from plants, but he went further, and extracted similar principles from the soil in which they grew, and then by beautiful experiments he showed that the rain-water dissolved many of these salts and other matters from the soil, and in this way enabled the plants to suck them up and absorb them. Those parts of the plants which he could not find in the soil he concluded came from the air, and, almost simultaneously, Hales (a celebrated English chemist) gave, by the method of experiment, a striking confirmation of these views. He determined the amount of water absorbed by the roots and that given off by the leaves of plants, and found it was through the agency of the little *stomata* or mouths, previously described by Grew, that plants breathe.

It is outside the present purpose to describe in any detail the advances made at that time in pure physiological science, but so intimately related to what has gone before, and so necessary the whole before it was possible for a Liebig, aided by the great animal chemists, Fourcroy and Vauquelin, to establish a new epoch in animal chemistry, was the work of Bonnet and Spallanzani upon animals, and Haller and Hunter's anatomical investigations, that it is most necessary at least that we should bear them in mind.

About 1770, Priestley observed that if growing plants were kept under a bell jar containing the bad air (carbonic anhydride) produced by burning or breathing, the air was thereby revivified and rendered fit for breathing again, and to support combustion. Although Black had even then discovered 'fixed air' or carbonic anhydride, Priestley did not understand the results he himself had obtained, and it was not until some time afterwards that the meaning of the process of plant-breathing was appreciated and understood.

The discovery of animal electricity by Galvani in 1789 lost nothing in importance by being accidental.[1] It is impossible to pay here even the most cursory attention to the toils of Scheele, Lavoisier, and Cavendish, and the men who continued their work after them. It is sufficient for the present purpose to bear in mind that all advance in physiological chemistry depends upon an ever-increasing acquaintance with pure chemical science, and that without those labours to which we have adverted, and the investigations of Nicholson, Davy, Dalton, and Gay-Lussac, Liebig's work would have been impossible. It is to a brief consideration of this work that we hasten. Since the days of Boerhaave nothing of any great importance beyond the facts we have mentioned was accomplished till the year 1828, when the celebrated German chemist, Wöhler, constructed urea synthetically. This was a tremendous victory for the chemists, for it had been loudly maintained that the substances elaborated in animal tissues were outside the constructive power of the chemist; it was said that although the chemist could analyse, he could not synthesise; he could destroy, but he could not create. But the artificial formation of urea showed how foolish are all preconceived opinions; indeed, it has been well said,[1] 'that fallacy is the child of preconceived opinion. Preconceived opinion is the pretended assumption by man of godly attributes which he does not possess. Man has no foreknowledge.'

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[1] Madame Galvani was skinning frogs for making a soup, while an electric machine was in work at hand; while the flow of electricity was considerable an assistant who was working the machine touched by accident with his knife the nerve of leg of a dead frog, whereupon the leg began to struggle and move; these facts were communicated to Galvani, and led him the discovery of animal electricity. (Buckley's *History of Natural* *ence*, p. 259.)

Liebig followed Wöhler, and gave extreme conviction by further discoveries to those previously effected. His earlier work was largely connected with a subject to which Davy had devoted much time and thought, namely, to the conditions upon which the growth of plants depend, and the relations of the composition of soils to such growths. It was not in these directions, however, that Liebig's work achieved the greatest success. Hitherto there had existed no definite methods ot analysis by which the composition of carbon compounds could be determined with anything like accuracy, but in 1830, Liebig introduced the plan of heating them in contact with metallic oxides, by which means they are resolved into simple products of oxidation which are readily determinable. It is upon this advance in chemical manipulation that the great chemist's fame chiefly depends. By the elaboration of a general method suitable to most compounds containing carbon and hydrogen, he placed in the hands of investigators an instrument of research more potent and more important than any corresponding discovery in the history of chemistry. Other chemists were not slow to take up, improve, and amplify these methods of analysis, and the results which have been achieved by their use constitute an epoch in science without a parallel. Through the agency we have described, the composition of most known substances has been determined, and chemists have been led to the discovery of hundreds, ay thousands of new compounds, many of which have been built up synthetically from their elements; many, even of those substances hitherto supposed to be inseparable from that mysterious and human-effort-paralysing vital force. 'So great was the impulse communicated by this perfection of method, that from darkness it has led to darkness again; for, in teaching us the composition of bodies, it has brought us to isomerism. When a new method of investigation shall impart a new impulse, we shall again emerge into light.'[1]

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[1] Thudichum. The Oration given at the 91st Anniversary of the Medical Society of London. *Medical Mirror*, vol. i., Nos. 7 and 8.

Chemical investigation can afford to pause so far as its development is connected with the sister science of physiology, which it has left far behind in the race of advancement. In the earlier days of Liebig, physiology scarcely merited its name, for up to that time physiologists had concerned themselves only with the study of anatomy and life functions, so far as this was possible without the aid of chemistry. It was a science of observation and deductive reasoning, while metaphysical speculations entered largely into its narrow sphere.

In his attempt to apply the processes of reasoning flowing out of chemical discoveries to the phenomena of life, Liebig experienced on all sides the resistance of that parent to fallacy, preconceived opinion, and, abandoning the opinions of his contemporaries, he devoted his teachings to a younger generation possessed of a more plastic mind. He saw how futile it was to struggle with a race of men of whom he was in apparent and such striking advance, and as for their metaphysical views, he argued that such must render men powerless in time to perceive the relations of cause and effect. He devoted himself with much earnestness of purpose to expose the unscientific methods of reasoning and research so prevalent at that time among physiologists, and ever advocated the principles of that inductive logic so ably interpreted by a man Liebig professedly admired, John Stuart Mill. Thus he gathered around him, in spite of all opposition—for truth was ever stronger than prejudice—a group of men who, by adopting and disseminating his teachings, gave rise by their labours to a new epoch in animal chemistry.

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[1] *Physiology, and its Chemistry at Home and Abroad,* by C. T. Kingzett and H. W. Hake, 'Quarterly Journal of Science,' January 1877.

It would be of the deepest interest to follow up the work thus originated; to watch the ever-growing wave of knowledge in its resistless advance; to study those lines of thought and investigation whose pursuit has led by rapid although imperfect advances to the idea of the beginnings of life and the germ theory of disease. It is true that men have here and there lost sight of those principles underlying all sound research, and have oftener plunged wildly into the mazes of uncerebrated research, the results of which, by their interconfliction, have hindered rather than helped scientific advance. But this is a phase of modern times that we have no intention of dwelling upon here; unfortunately, there will be only too much opportunity and necessity for its revelation in future chapters. Here let us consider Liebig's philosophy somewhat more in detail. He assumed the existence of a vital force, or whatever we choose to call it—say, an agency—powerful to develope from the seed the plant, and from an egg the bird; but at the same time he acknowledged above all men, and insisted upon the truth of his admittance, that the actual processes of life, with all their complications of function, were based upon the same laws which operate between matter and force in the chemists' laboratory.

The history of all science shows that it developes, first, by the accumulation of isolated facts; secondly, by the discovery of determining influences, and of certain relations between those facts; thirdly, by the deduction of general laws from larger series of observations than those upon which special laws depend. Finally, it becomes possible from given conditions to predict the next states of certain forms of matter. To these rules physiological science makes no exception. The phenomena of life stand like those of dead or inorganic matter in certain co-relations which are determined by specific causes; and it is only in the light of a knowledge of these causes and their nature, that the processes of life can be ascertained. Such a search constitutes the most important problem in physiology, for by it is to be discovered the mutual dependence of the vital phenomena. It is true that anatomy here is of great avail, but, unaided by chemistry, its discoveries have comparatively little meaning; not only is the anatomical method insufficient of itself, but it is subordinate to the chemical method. Such were the opinions of Liebig.

There are those who hold the opinion that in life there is something which renders negative all our conclusions drawn from laboratory experiments, and nullifies all our hypotheses of functions, but they are men who fail to grasp thoroughly the conditions upon which life depends. The vital force, compound by nature as it is, partakes in its component parts of the same character as the chemical force, inasmuch as it only acts when the particles are more or less at infinitively short distances from each other. Life itself is the expression of the metamorphoses of the animal tissues; in other words, man lives by virtue of certain changes of matter incessantly going on in his body, and what is chemistry but the study of the laws of changes of matter? Surely, it has no further meaning.

The dogmatism of churches and ages, the unreasoning and prejudice always associated with ignorance and untrained and unscientific minds, have done their worst and they have done their best, but what explanation of life, health, and disease have they given? None! They have told us that nervous force emanated from a nervous system, and that cooling substances are astringents; they have invoked superstitions and conjured up groundless faith in an agency whose function they could not define, and of which they thought it was blasphemous and wicked to enquire. This dogmatism, this circumscription of language, received from Kant in his earlier writings long ago, what in more recent days it has received and merited at the hands of John Stuart Mill. And, although churches still boast their superstitions under a cloak of religious faith, and although men's minds are still tainted with that bias against improvement so common to the savage, the further pursuit of science will overpower and destroy it all in due time. We may not live to see it, but it is as inevitable as the daily setting of the sun.

But to return to our more immediate theme. The object of physiological chemistry, then, becomes the reduction to general laws of those phenomena which, in their multifarious co-relations, constitute the functions of life. To prosecute this study with hope of success, it is essential that we should first become acquainted with the composition and constitution of those substances which are elaborated in the various tissues, organs, and fluids of the living body, and of which these are themselves constituted. It is only by means of such knowledge that we can be enabled to trace out the intricate concatenations of the various parts of the animal body, and of those metamorphoses which are constantly in process in the living laboratory. Such studies are as necessary to physiology as it is to ascertain the composition of hydrochloric acid and chalk, before we can explain any action they may have one upon the other.

From what has gone before, it will be apparent that the method to be pursued in the study of pathology is identically of the same order as that requisite for use in physiology, and the results of these parallel investigations appear as the expressions of health and disease. Mr. John Simon has well expressed[1] this truth by describing pathological results as the 'morbid declensions' from the 'normal chemical standards' of physiology.

While the method to be pursued in such studies is plainly visible, and when the results to be attained are so all-important to the prosperity and health of man, it is surely matter for deep regret that there are but very few men availing themselves of it. Not only is this true of England; it is true in a different measure of Germany, France, and other nations. The reason for this is not far removed. It is true that in the science of physiological chemistry there are pending matters for research which might fairly be undertaken by men of ordinary attainments at very little expense; but there are many questions (and these are the most important of all) to be solved, which are much further removed from the abilities of the untrained mind, and which demand for their elucidation means and time at the command of but few private individuals. This is notorious and acknowledged. I contend, however, that even were there men who have the time and the means whereby to grapple with these problems in science, there is not, at least in our country, any system of training by which such men find it easy to qualify themselves for such studies and researches. The result is, that the work is to a large extent neglected, or, when undertaken, from the reasons stated, the results attained are often lamentably worthless or deficient. The truth of this statement is not to be gainsaid; it is a matter of everyday experience, and to those who are conversant with recent scientific literature, these remarks will furnish no matter for surprise. It were easy to substantiate these statements, but it is unnecessary, it having been already done.[1]

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[1] *Reports of the Medical Officer of the Privy Council, &c.* New Series, No. 3, p. 8.

On the successful pursuit of the study of animal chemistry, all medicine rests. Diseased livers, brains, hearts, and lungs; organic and chronic diseases; cholera, typhus, and typhoid fevers; all these and hosts of other diseases and disorders, no matter what their causes or their origin, have something in common. All diseased organs and all morbid processes speak of chemical changes and processes different from those actuating and controlling the organs, tissues, and fluids in health, and of necessity, therefore, curative and preventive medicine must in the main have its basis in a knowledge of histo-chemistry. At present, medicine is rather an accumulation of experiences than a natural science, whereas it ought to occupy the leading place in science, in fact shine out as that ultimate focus in science upon which and towards which all other science sheds its rays of light, and to which human efforts should be above all things directed.

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[1] See Essay in *Quarterly Journal of Science*, by C. T. Kingzett and H. W. Hake. January 1877.

Many are the medical men who say, and say with considerable show of reason, all this is very true, but if we stay in life to study animal chemistry and the chemical changes underlying pathological processes, our patients will die in the meantime. It is true we are terribly overmatched by disease, but still we can do something to stay its progress, and to that something we must devote ourselves. Who then is to prosecute the science, if the medical men will not or cannot? The chemists? Unfortunately, physiological chemistry is not taught as an ordinary part of the science, and chemists who ordinarily devote themselves to research, find such labours too tedious or too unprofitable in results, and so the work is left undone for the most part, and in the meantime disease ravages mankind, and demonstrates in a terrible manner how futile are our strongest efforts to stay its progress. Still something might be done if the system of teaching at medical schools were improved.

Animal chemistry finds no advocates at our Universities and public schools, and is not embraced in their curriculum; it is professedly taught, however, at our medical schools; but if one takes the trouble to enquire into this teaching, one is rudely shaken in their beliefs. What is really taught is not animal chemistry, but a certain number of facts. The students are made acquainted in an empirical manner with the ordinary methods of separation employed in the qualitative analysis of substances, which, for the most part, do not occur, and have little to do with the animal body; they are taught certain tests for poisons of various kinds, and are put through, it may be, a few exercises in quantitative analysis of inorganic substances. Their learning is crowned by cramming a further number of facts regarding the blood, the urine, and bile, and imbued with this knowledge they enter on their medical career. This is not the way to teach animal chemistry, and the teachers are to a large extent incompetent to fulfil this task. To appreciate and to pursue this study, a previous knowledge of ordinary chemistry, and a wide one too, is requisite; moreover, a more than superficial acquaintance with physics is required, and, for most purposes, an understanding of human physiology. Then, again, facts do not constitute a science; science is constituted of principles; and from our teaching, and our text books, and our teachers, from none of these do medical students of to-day learn these principles. Of the teaching and the teachers we have already spoken; as for most of the text books in use, not only in this country, but abroad also, they are the merest compilation of facts—facts picked up here and there and arranged together in chapters 'specially designed for the medical student.' Alas! for the medical student; he finds no philosophy in them, but only a certain number of statements with which he must make himself familiar without understanding them; a certain array of facts which he must learn as he learnt dates of historical events when a boy at school; facts without a binding link; statements possessing no exhibition of relation; the whole devoid of connecting principles and a scientific philosophy. In the face of what has been shown, is a man having such knowledge as he may acquire at our medical schools well fitted to understand the processes of health and disease? has he any power to add to our knowledge of these things?

Moreover, the books of the day have another grave fault; they are not only imperfect so far as they go, but they do not go far enough. Recent and the most important scientific researches find too often no mention, or when they do, the accounts are, not rarely, worse than useless; they mislead from their inaccuracy; they injure men by the prejudice they exhibit.

It is quite true that one half of the world does not know how the other half lives. There are people who talk of the republic of science as others once talked of the republic of letters. Alas! for the republic of science. In art, in literature, in law, in medicine, in fact, probably nowhere at the present time is there so much bickering, jealousy, and conceit as in the infant republic of science. Not only is this true of private life; there slander, machinations, and prejudice are exerted to the full. This is bad enough, but it is too bad to carry this sort of thing into public life and scientific literature, and yet it is done, and on a glaring scale too. The consequence is that our literature loses in value; the teaching of the day is frustrated by external politics; the whole system of science receives a serious check.

Boast is made of the rapid progress of science. Bah! it is untrue. Science never did, does not, and never can make rapid strides. Relatively, progress may be rapid, but it is only relative to times when progress was much slower. But if men would only throw aside, at least in certain walks of life, jealousy, prejudice, and partiality, and unite in a true and honourable republic of science, how much better would it be for science. There was never a finer example set by man than that taught to the disciples of alchemy, 'Ora! Lege, Lege, Lege, Relege, Labora et Invenies.'[1]

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[1] See Mr. Rodwell's *Birth of Chemistry.*

CHAPTER II.

LIFE: FROM A CHEMICAL POINT OF VIEW.

For the purposes of the present work it is not requisite to enter at all deeply into the anatomy of the human body. In order to show the processes according to which man 'lives, moves, and has his being,' it is but necessary to regard him as a conscious machine or an automatic instrument. Nor is it necessary to have regard to man's place in nature beyond its enunciation. Possessed of conscience, will, and power, he finds himself as the creature of a generation composed of beings like himself, exhibiting certain relations among each other. Of the individualities or character we shall have a little more to say later on; it will suffice here to recognise the individuality of man. This individuality, controlling the whole life-actions, is unfortunately almost universally ignored, or where it is not ignored, it is not rarely misinterpreted. The doctrines of evolution and survival of the fittest, and all those thousand minor laws which in view of the teachings of men like Darwin, Spencer, Wallace, and others, we hold to be true of lower forms of animal life, are true also of man. He is the resultant of a thousand conflicting predestinations and emotions; the focus of predispositions and circumstances that have been in action for ages. Where then lies the difference of individualities? Partly in the brain power; partly in the individual organs of the body; partly in the general relations these bear to one another, and the whole of them to the brain power. For, in a general sense, all men are constituted alike; the philosopher Aristotle, Homer the poet, Mill the logician, Napoleon, of iron will; all these, and all men, are in their physiological form alike. The characters and individual powers of these men are to be traced not so much to any individual difference of form of the various organs of the body, but rather to qualities possessed by some or all of those organs; qualities which have a quantitative expression, but whose meaning is hidden deeply in the tissue of which the organs themselves are composed

To return, however, to our consideration of man as a conscious machine having complicated functions, that is to say, a machine powerful to do muscular and mental work by virtue of a force generated *in situ*, and guided by will. It is a fact of the deepest meaning that the food which we eat takes part in that with which we think, and the body having once attained a full development of form and size, food henceforth represents one side of the equation of life; on the other side is represented the history of our life.

It is not intended to study those processes of development and growth antecedent to maturity; it is sufficient to bear in mind that there is a beginning, an embryo phase, and intermediate stages of life. But from the beginning there is an inherent power in the life substance, call it protoplasm, bioplasm, or what we may, which determines the evolution out of its own elements, of tissues and organs, and which constantly regenerates itself, so to speak, from the food presented to it.

Hence we may fairly say that the human body is a mere apparatus by the agency of which man lives in another sense, viz. the mental or intellectual sense. The study of the construction of that apparatus constitutes the science of physiology; the life which is maintained in and by the human body is the result of chemical changes incessantly occurring in the matter of which the tissues and organs and fluids of the body are constituted. The same life depends for its continuation upon the food which is taken into the body, and from which there are elaborated new fluids, and new tissue to replace that previously lost by the act of life. When the processes we have alluded to, follow an inherent determinated direction, they may be conveniently summed up under the title of physiological chemistry; but when declensions arise the processes are morbid, and the result is disease: this study constitutes the science of pathological chemistry. Together, these two subjects are included in the expression 'animal chemistry.'

Let it not be thought, however, that there is in this description any desire to hide away that which we cannot explain. In life, anatomy has its share and chemistry and physics have also their parts. All these subjects, however, cannot be considered together, and this statement is here made in order to avoid the stigma which Henle attached by his criticism to Liebig's work on 'Animal Chemistry.' Henle wrote: 'With consummate skill he (Liebig) draws a few crystalline threads out of the tissue of life, and holds them up to admiration as the share of chemism; he then throws us the lump which he cannot unravel as the share of vitalism.'

Now according to the above showing, a man requires to take daily a given amount of food properly prepared by cooking and otherwise. This is comminuted in the mouth and is there mixed with saliva; as it arrives in the stomach it is further mixed with various fluids and secretions, including gastric juice, bile, pancreatic juice, and so on, and here digestion partly occurs; it is completed in the smaller intestine, and the undigested and valueless part of the food is excreted as fæces. The chyme and chyle thus formed are conveyed by proper vessels to the blood system, and by means of the heart's action are distributed throughout the body. As the blood circulates through the system, the various organs assimilate from it the nutriment they require to reconstruct themselves and keep in working order; at the same time they yield to the blood the soluble effete products of life; products resulting from decomposition and change, upon the carrying out of which their very functions depend. In this way the blood passes on to the kidneys, through which it filters as it were, and allows the worthless part of it—that consisting of the excrementitious products—to be removed as urine. Simultaneously with these processes occurs that of respiration, an act which depends upon the inspiration of air and its passage through the lung tissue into the blood. This oxidising effect is carried out by the blood in all parts of the body, and in return that fluid takes up carbonic acid—a product of oxidation—which is afterwards duly eliminated through the lung tissue also, viz. at the moment when the blood arrives there for a fresh supply of oxygen. It would also appear that man undergoes a cutaneous respiration, although in a smaller degree, much water and certain other matters being eliminated through the skin. Each and all of these processes will be fully considered hereafter, and this résumé is given merely to demonstrate, at the outset, how great a share chemistry takes in life. It concerns itself with the nature and composition of the food taken; with salivary, stomachic, and intestinal digestion; not merely so far as these processes themselves are concerned, but also with the composition of the various animal juices taking part in them, as well as with the very composition of the organs which secrete the said juices. Then again, chyme, chyle, lymph, blood, have each their chemistry and interrelations, and, what is more important, the act of respiration is essentially a chemical one. This then has to be studied, as also the methods by which the organs and tissues of the body oxidise and repair themselves. That these organs, such as the brain and lungs, have a chemistry, is a matter which has only of late years received the attention the subject merits, for, as previously stated, there were in past times not wanted men who denied, or at least did not recognise, the fact of their chemical composition. Finally, there is the chemistry of bone and muscle, and of the various excrementitious matters, such as sweat, urine, fæces, and breath.

Regarding the various subjects just enumerated, our chemical knowledge is both small and great; that is to say, it is great in itself, but does not nearly represent the whole possible knowledge. The chemistry of digestion particularly is but little understood, whereas there can be no doubt that an increased knowledge of the composition and properties of those specific ferments which take part in it, would lead to an immense gain, not only for human physiology, but also in our appreciation of the meaning of fermentation as a general phenomenon.

With the subject of ferments is intimately connected one which of late years has attracted a predominating amount of attention, namely, the germ theory of disease and infective processes; and, once arrived at this stage, we verge upon the beginnings of life. It cannot be doubted that for the future progress of our knowledge of these questions we must look more to chemical science than has been done in the past. It is too true that our slight knowledge of the composition and inter-relation of bodies occurring in the human system, and of the processes by which they are built up from food and transformed into ultimate products after fulfilling the vital functions, only shows how much yet remains to be learnt. It is soon perceived that we stand but on the threshold of knowledge, and many must be the thinkers and workers, and generations upon generations will pass away, before the processes of life shall stand forth entirely revealed; before it shall be known how, from a few simple matters tolerably well known themselves and administered as food, is built up man with his marvellous and beautiful structure, with his power of thought, feeling, and action. That such a time will come scientific men have no doubt; we shall know more to-morrow of the sun that shines to-day!

There is darkness around the vital phenomena, but that darkness exists only because science has not yet attacked nature and illuminated it sufficiently by its discoveries, waiting to be effected in these directions.

There will always exist men who will doubt the possibilities of science; who will call in question matters which have been established as truth for all time, just as men, even to Bacon, rejected the doctrines of Galileo, and as Leibnitz spurned the philosophy of Newton on gravitation. But, in spite of all, the sun of science will dispel the morning cloud of ignorance and prejudice, and will unfold to us the laws of nature unbiassed by the poetry of man's mind and free from the superstitions of churches.

CHAPTER III.

CHEMISTRY AS APPLIED TO PHYSIOLOGY AND PATHOLOGY.

ALTHOUGH this work pre-supposes a certain knowledge of chemistry on the part of its readers or students, it may yet be desirable to make a few observations regarding the classification of carbon compounds, inasmuch as the greater part of the human body is made up of such substances. In doing this, it is not proposed to consider the reasoning upon which the various systems of classification are based, nor to comment upon the relative values of them, but rather to supply an explanation, brief though it be, of terms and names which will be found in use throughout this work. Moreover, while a system of classification is all-important in certain branches of pure science, it serves a far minor although important service in a science like that of which we are treating, and for this reason; that the function of physiological chemistry may be said to consist in the elucidation of those processes by which life with all its many side-issues and declensions is maintained. In this study, chemistry is competent to teach us how from certain substances given as food, the constituents of the body are produced; and again, how these products suffer subsequent change, and give rise to other and excretory substances. In other words, the physiological chemist, having regard to his ultimate objects, seeks to determine the relations existing between different substances supplied to, found in, and excreted by the body. It is upon a knowledge of such relations that he is enabled to understand the processes of life ; that, in fact, he is able to hope for the attainment of his object. In such a search it is not requisite, at least in the present state of the science, to consider the chemical constitution of bodies in greater degree than that which is requisite to show how this substance is produced from that substance, or this other compound may give rise to that other compound. In short, chemistry as applied to physiology is a means of working out dynamical equations in which certain masses are dealt with on the one side, and on the other, lesser sums, the total of which is equal to the original mass. To instance our meaning, let us deal with a body like fat, which is known to yield glycerine and fatty acids when decomposed in a certain manner. The chemist has a particular interest in determining, not merely the general properties of these substances, but also in seeking to ascertain their actual constitution, or the manner in which the atoms entering into their composition are arranged. By the application of certain tests he can tell the general nature of substances, and can place them by the side of others of similar characters, and believed by him to have a corresponding or comparable constitution. True that such a method has its meaning, even in physiological chemistry, but what is more directly important to the physiological chemist is the quantitative determinations of the total products obtained in the particular decomposition of fat referred to, and such other instances.

The chemist may obtain one product upon which he may devote unlimited study to ascertain its properties, general nature, behaviour to reagents, and constitution, whereas the physiological chemist should seek rather to devote his attention to all the products, until not only the individuality of each is established, but until their sum is equal to the mass of matter from which they are originally produced.

Again, we shall see in another chapter that, chemically considered, leucine is an amidated fatty acid, and chemists have made themselves well acquainted with it, its character and constitution; they also know it to be obtainable from albuminous substances, and further know it, when thus prepared, to be identical with the leucine prepared by artificial synthesis. But this is not enough for the physiological chemist, who seeks to ascertain exactly its amount and the nature and quantities of all other substances by which it is accompanied when made from albumin. Further, it is important for him to know whether it can arise from other sources in the body, because, if not, he is at once able to indicate its origin under any particular set of circumstances, and, indeed, is in a position to make a sort of generalisation. Now, of late years, there has been introduced into chemical teaching the so-called 'structure' hypothesis of carbon-compounds, under which these latter are represented as structures comprised of constituent atoms arranged graphically. This graphical arrangement is arrived at from a knowledge of the way in which substances decompose when subjected to particular processes. That is to say, if they yield by some process a particular substance, this is considered as sufficient evidence that they contained in their structure a particular group of atoms; and so far so good. But many chemists go further than this, and say not only that such and such a group is present, but also that it is present in a certain position. It is this last-named assumption that is so extremely unprofitable and unmeaning, particularly for physiological chemistry. Being purely hypothetical, it has no place in true science or healthy logic. Let us try to indicate how far logical reasoning enables us to indicate the constitution of substances. Glycocholic acid, when decomposed with dilute acids or alkalies, yields cholic acid and glycocine, and as the process employed is a mild one, and as these are the only products, it is inferred that in the original molecule of glycocholic acid, these substances, or residues of them, were co-existent. But even this is mere inference, because if glycocholic acid be submitted to other processes it yields other products, and applying the same reasoning, we make the *reductio ad absurdum* that this substance contains, as primary or proximate nuclei, such a number that the sum total of their elements is greater than the amount of substance operated upon.

To say that because a certain substance yields certain other substances by a particular mode of decomposition, therefore residues of these latter must have been present in the parent molecule, is an assumption having admittedly more or less plausibility and even usefulness, but it is an argument which must not be pushed too far, or at least must be limited by very clear definitions. This is so, because it appears equally good reason to say that, since by acting upon a particular substance with another substance a third one is produced, and is unattended with other substances, therefore this new substance contains groups or radicles previously contained in the two separate ones; but such reasoning as this soon leads us into a fog, since very often the same substance may be prepared in half-a-dozen different ways, and from substances of such different natures that obviously these could not contain a common group. The fact of a chemical reaction cannot be exceeded, and a chemical equation may or may not express the whole truth. When carefully thought out, it becomes clear that chemical constitution is a phrase of little meaning; it is a something conceived to have a relation of some sort with the substances from which and the manner in which a body is produced, and again, the substances into which and the process by which it may be resolved. In short, and curiously enough, the chemists who most bravely defend the 'structure' theory of carbon compounds, have latterly assumed a position which indicates its own indefensibility. For example, benzene, when submitted to various processes, is capable of yielding hundreds of different substances. 'Structure' chemists may write benzene as a graphical arrangement of carbon and hydrogen atoms, in which each carbon atom is directly united with a hydrogen atom, and continuously with all the other carbon atoms. But putting aside the illustration for what it is worth—the particular figure varying with the author—their structure amounts to the recognition of the fact that in benzene there are six carbons united with six hydrogens (C_6H_6) and amounts to nothing else. 'Structure' chemists are not without a kind of reasoning in defence of their propositions, but it is a sort of reasoning not comprehended in the science of logic. In fact, the structure theory of benzene amounts to nothing more or less than the statement, made in a particular way, that benzene consists of two elements, and that if a certain quantity be taken and submitted to the action of a certain quantity of other substances, it may yield a number of substances, but supposing that from these the benzene could be got back again, then the amount would be equal to the original quantity taken. In other words, it is true that, given a mass it is possible to break it up into parts the sum of which equals the original mass. Vary the means employed to break it up, and with them the parts or products differ also.

For the purposes of physiological chemistry, it is sufficient to understand the meaning of a chemical reaction, and it is desirable that a chemical equation illustrating such reaction should be as far as possible a mathematical equation in the sense that the other side should specify not one particular product, but embrace all and indicate their relative amounts. These amounts should be equal to the acting masses represented on the first side of the equation.

The Chemical Principles and Educts of the Body.—It will be seen from the contents of the following chapters, that a large number of the substances found in the body are of huge molecular proportions, and do not admit, so far, of any reasonable classification. Thus it will be shown that there are reasons for regarding hæmatocrystalline, or the colouring matter of the blood, as a distinct chemical individual of probably greater complex constitution, than fibrin. So complex indeed must be its constitution that even one of its decomposition products—hæmatin—is of undetermined structure. Again, the immense variety of albuminoïds cannot be formulated upon a general type, while many of their decomposition products require much more study before they admit of classification. Chemical researches have already led to general formulæ for many of the brain principles, including the phosphorised substances allied to lecithine, $C_{42}H_{84}NPO_9$, but of the constitution of the cerebrines and other substances, next to nothing is known with any degree of certainty.

While, therefore, it is impossible to comprehend many principles and educts in any system of classification known to chemical science, the same cannot be well said of the better known simpler substances which are not peculiarly of animal origin, and they embrace representatives of almost every type of chemical substance.

The majority, however, of these classifiable bodies consist of alcohols, acids, amidated acids, and amines.

Hydrocarbons, or compounds consisting exclusively of carbon and hydrogen, do not occur in the body, nor are they contained in the food ordinarily partaken of by man. One may well conceive that under the universal condition of oxidation which obtains in the living body, it would be, perhaps, impossible for any hydrocarbon to permanently exist, even if elaborated therein.

The alcohols, chemically considered, are substances containing replaceable hydroxyl (HO); or they may be regarded as substitution derivatives of the hydrocarbons; thus ordinary ethylic alcohol may be written $C_2H_5(HO)$, which signifies that it is the hydrate of ethyl. These compounds are the analogues of the metallic hydrates, and extend to and embrace many carbohydrates belonging to the groups of starches and sugars.

Many alcohols, therefore, enter into the composition of our food, and not only so, but they are also probably elaborated within the body itself, in some cases by a process of hydration operating upon suitable originating substances. In this way all glucosides yield sugar, and many starches also yield sugar.

Mercaptans, or thioalcohols, of which ethylic sulphydrate (C_2H_5HS) is an example, do not occur, so far as is known, within the body, nor is it possible to say whether the sulphur contained in some albuminous substances exists in combination in some such form.

If any of the starches constitute ethers (as the anhydrides of the alcohols are termed), then these form not only part of the food, but are also found in the body, as for instance, glycogen ($C_6H_{10}O_5$) in the liver. The ethers are converted into alcohols by heating with water or alkalies, thus ethylic ether becomes ordinary alcohol as follows: $(C_2H_5)_2O + H_2O = 2C_2H_5(HO)$. Glycogen under the same treatment takes up water and becomes sugar.

But the true constitution of the bodies known as starches is far from being accurately determined, and in the chapter on carbohydrates, it will be shown that some forms of starch are regarded as aldehydes, or compounds intermediate between the alcohols and the acids.

The aldehydes are regarded as hydrocarbon derivatives in which hydrogen has been substituted by a monatomic radical group $(C^{iv}O''H)'$. Thus ordinary alcohol gives rise to the formation of ethylic aldehyde when subjected to partial oxidation, $CH_3CH_2OH + O = CH_3(COH) + H_2O$. By further oxidation acids are produced, as for example :—$CH_3(COH) + O = CH_3CO.OH$—this equation represents the oxidation of aldehyde into acetic acid.

It is thus seen that in an ultimate sense, acids may be regarded as oxidation products of hydrocarbons, in which hydrogen is replaced by a monad carboxyl group (CO.OH), and as there are different series of hydrocarbons, so there are various series of acids. They all furnish metallic salts, haloid salts, ethereal salts, amides, and whole series of other compounds of more peculiar interest to the chemist.

Of the acetic series, a large number of members occur in the body, and are obtained by processes of decomposition from various substances of animal origin. The acetic series is derived from the hydrocarbons of the general formula C_nH_{2n+2}, and is represented by the general formula $C_nH_{2n+1}CO(OH)$. It consists of homologous members, differing by CH_2, as shown by the following examples.

Methylic or Formic acid	$HCO(OH)$.
Ethylic or Acetic acid	$CH_3.CO(OH)$.
Propylic or Propionic acid	$C_2H_5.CO(OH)$.
Tetrylic or Butyric acid	$C_3H_7CO(OH)$.
Pentylic or Valeric acid	$C_4H_9CO(OH)$.
Hexylic or Caproic acid	$C_5H_{11}CO(OH)$.

All these may be obtained from animal sources, and notably by the oxidation of albuminous and other substances.

The following are also of interest to the animal chemist, and belong to the same series.

Palmitic acid	$C_{15}H_{31}CO(OH)$.
Margaric acid	$C_{16}H_{33}CO(OH)$.
Stearic acid	$C_{17}H_{35}CO(OH)$.

The Acrylic, or $C_nH_{2n-1}CO(OH)$ series of acids, derived from the C_nH_{2n} hydrocarbons, is represented by oleic acid, with which we shall make ourselves acquainted in other chapters.

The Benzoic, or $C_nH_{2n-7}CO(OH)$ series of acids derived from the C_nH_{2n-6} series of hydrocarbons, is represented by benzoic acid, $C_6H_5CO(OH)$, and other substances.

Again, the Acetic series gives rise to a secondary series, known as the Lactic, and of the general formula $C_nH_{2n}(OH).CO(OH)$; while from the Benzoic series, another secondary, Salicylic or $C_nH_{2n-8}(OH).CO(OH)$ series may be derived.

The juice of flesh contains two isomeric lactic acids, one of which appears to be identical with ethylenic lactic acid, while the other, sarcolactic or paralactic acid, as it is variously called, is distinguished by its power to direct polarised light to the right. Its products of oxidation are identical with those derived from ethylidenic lactic acid.

Among the many derivatives of the acids, none are of so much interest to physiological chemistry as the amides. Artificially, these substances present no difficulty in formation; thus they may be readily obtained by the action of ammonia on the acid chlorides, as for example:

$$CH_3COCl + 2NH_3 = CH_3.CO.NH_2 + NH_4Cl,$$

or by distillation of the ammonium salts of the acids; thus,

$$CH_3CO.ONH_4 = CH_3.CO.NH_2 + OH_2.$$

Of course each series of acids gives rise to its own amides, which may be viewed as compounds formed from the acids by replacement of the (OH) group in the carboxylic group by the monad residual radicle (NH_2), (amidogen derived from ammonia, NH_3).

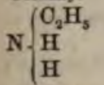
The monobasic acids yield only normal amides, while dibasic acids give both normal and acid amides, or amic acids as they are termed.

In the chapter on albuminous substances it is shown, that in the decomposition of these bodies by a process of hydration, a large number of amides and amic acids are obtained. There are representatives of these substances also in the urine, notable among them being hippuric acid (benz-amido acetic acid).

The only other class of bodies we need notice here is the amines, which are viewed as being derived from ammonia by the substitution of hydrocarbon groups for hydrogen. The amines, or compound ammonias, as they are also termed, may be grouped into three classes, namely monamines, diamines, and triamines.

Thus we have among others the following monamines:—

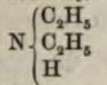
Primary.



$$N\begin{cases}C_2H_5\\H\\H\end{cases}$$

Ethylamine.

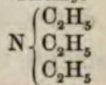
Secondary.



$$N\begin{cases}C_2H_5\\C_2H_5\\H\end{cases}$$

Diethylamine.

Tertiary.

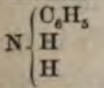


$$N\begin{cases}C_2H_5\\C_2H_5\\C_2H_5\end{cases}$$

Triethylamine.

We have also:—

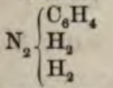
Monamine.



$$N\begin{cases}C_6H_5\\H\\H\end{cases}$$

Amidobenzene.

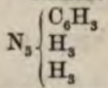
Diamine.



$$N_2\begin{cases}C_6H_4\\H_2\\H_2\end{cases}$$

Diamidobenzene.

Triamine.



$$N_3\begin{cases}C_6H_3\\H_3\\H_3\end{cases}$$

Triamidobenzene.

These amines are well represented in physiological chemistry by urea or carbamide $CO(NH_2)_2$, and the large number of derivatives to which it gives rise, as also by trimethylamine obtained from various animal substances by distillation. As another representative, although of a more complex kind, we may example neurin, or the ammonium base obtained in the decomposition of the phosphorised principles of brain matter. All these organic ammonias strongly resemble ammonia in their properties, combining directly with acids to form salts, by treatment of which with oxide of silver the corresponding hydrates are obtained. Thus—

$$C_2H_5.NH_2 + HCl = C_2H_5.NH_3Cl.$$

and

$$2C_2H_5.NH_3Cl + Ag_2O + H_2O = 2C_2H_5.NH_3.OH + 2AgCl.$$

The hydrates obtained in this way are caustic substances, exhibiting many of the properties of their analogues, the caustic alkalies.

Chemical Changes Occurring in the Body.—The chemical decompositions for ever occurring in the living body are all included in two processes, viz., those of hydration and oxidation, that is to say, they are decompositions depending upon the assimilation by substances of the elements of water, or upon the action of oxygen. These processes occur of course separately, but they may be, and often are, associated in succession. They are of sufficient importance to merit some special consideration in this place, and glancing lightly over the ground which is covered more particularly in the various chapters, a number of instances of hydration and oxidation may be *en passant* referred to. For instance, the starch of food is, in the mouth and stomach, transformed into sugar by the assumption of water, an assumption directly caused by the unexplained ferment-like or contact-like power of ptyaline. Again, the amyloid-substance of the liver is supposed to undergo a similar change, or, yet again, fats in course of digestion are likewise split up by hydration into fatty acids and glycerine. In pathology, the hydration process is apparently of yet greater importance, thus, for example, in softening of the brain, one of its principles suffers disintegration in this way. The following equations show these changes, which are seen to depend upon the direct assimilation of water by the bodies thus changed.

$$C_6H_{10}O_5 + H_2O = C_6H_{12}O_6$$

$$C_3H_5\begin{cases}C_{18}H_{35}O_2\\C_{18}H_{35}O_2\\C_{18}H_{35}O_2\end{cases} + 3H_2O = C_3H_5(HO)_3 + 3C_{18}H_{36}O_2$$

$$C_3H_5\begin{cases}C_{18}H_{33}O_2\\C_{16}H_{31}O_2\\HO(OPO)C_5H_{13}NO\end{cases} + 3H_2O = C_3H_9PO_6 + C_5H_{14}NO + C_{18}H_{34}O_2 + C_{16}H_{32}O_2.$$

This assumption of water takes place, in numerous instances, at the ordinary temperatures, but for other cases, a more or less elevated temperature is required. This latter condition is, of course, provided in the animal body also. Changes by hydration may result from mere contact with water of the bodies to be changed; in many other instances they occur by the intermediation of a third body, such as dilute acids or other substances, partaking of the nature of a ferment or zymase. The specific manner of this intermediation is undetermined. It is by a process of hydration that albuminoïds in the stomach are changed into peptones, and again, it is by a similar process, perpetuated further, that these are decomposed into such proximate nuclei as tyrosin, leucine, &c.

Oxidation, as a process happening outside the body, or in the laboratory, is very well understood. There are degrees of oxidation as there are degrees of hydration, and these depend upon the nature of the oxidising agent and the conditions under which the process is effected. Thus the products of the oxidation of turpentine, for example, differ according as the oxidant be air, or nitric acid, and so forth. It is so-called 'limited' oxidation that is of peculiar import in studying the chemistry of animal and vegetable processes; in other words, it is oxidation by air which chiefly concerns us here.

In some cases hydrogen is removed, having combined with the oxygen of the air to form water; this happens with alcohol as follows:—

$$C_2H_6O + O_2 = H_2O + C_2H_4O_2;$$

or the reaction may go further in the body, perhaps, and give rise to water and carbonic anhydride only; thus—

$$C_2H_6O + 7O = 3H_2O + 2CO_2.$$

Or, again, oxygen may not only remove hydrogen from substances in this way, but may also attach itself simultaneously. It is doubtful whether such a state of things ever happens in the animal system, but it is quite conceivable, inasmuch as one may realise it in the laboratory.

Further, oxygen may resolve large molecules into simpler ones, with the elimination of water and the production of oxidised compounds. Thus—

$$C_7H_6O + 3O_2 = H_2O + C_3H_6O_2 + 2C_2H_4O_2.$$

Here, triethylcarbinol is resolved into propionic and acetic acids, whilst water is also formed. In other cases oxygen is simply added on to the substances exposed to its action, aldehyde becoming in this way acetic acid,

$$C_2H_4O + O = C_2H_4O_2.$$

As with hydration, so also with oxidation, it may be said that the milder the means resorted to, the more closely allied are the products to the original parent molecules. The remarkable thing to be noted here, however, is, that whereas out of the body it is difficult to make air or oxygen itself effect certain decompositions, stronger reagents being required, yet, in the body, oxygen is the only substance which is utilised for purposes of oxidation. There is this difference to be observed, which throws some light upon this curious fact, viz., that the substances which undergo oxidation in the body are probably the simpler molecules which have been first produced from larger molecules by hydration; these larger molecules, being for the most part colloidal in nature, offer, as a rule, less resistance to processes of change than substances of a crystalline character, to which class most of the substances treated in the laboratory belong. Moreover, the simpler nuclei, which undergo oxidation within the body, may be in *statu nascendi*, that is to say, just broken off from the parent substances, and scarcely settled down into their next forms, and it is notorious that bodies in this state of being are peculiarly liable to undergo oxidation under given conditions.

No doubt, within the body these processes of hydration and oxidation may occur successively so quickly as practically to occur together, or they may even literally occur together. We have an example of this in the laboratory with acetylene, which, under these combined influences, becomes acetic acid,

$$C_2H_2 + O + H_2O = C_2H_4O_2.$$

It is too often ignorantly imagined, and also stated sometimes, that the animal function is mainly or entirely one of analysis. The act of synthesis is conceived to reside almost exclusively in life of a vegetable character. This is erroneous, for we find most complicated synthetical acts going on in the animal body itself, and surely the very existence of brain matter and hæmato-crystalline is sufficient proof of this. To appreciate the truth of this it is only necessary to bear in mind that life can be sustained upon food made up of albuminous compounds, fat, starchy matters, sugar, and water; and hence it must be by reactions occurring between these substances, or the products produced from these within the system, that the brain-matter and other principles are evolved. Not only is it so with brain principles, but also with many of the constituents of the bile and the blood, &c. But of the exact processes by which such syntheses are effected, we may be said to know next to nothing. One of the most evident of these synthetical acts is the formation of the solid tissues themselves, mainly composed as they are of albumin in one or other form. Fibrin, or the flesh of animals, when eaten as food, suffers a kind of analytical change in the stomach; it is changed, as we know, into soluble peptone-substance, which, by its solubility and ultimate state of division, admits of being absorbed into the circulating fluids of the body. By and by, however, the peptone-substance is synthetically changed into solid albumin again, and, as such, goes to form muscle and so forth. Much more marvellous, however, is the power existing in the protoplasm of brain matter—the power by which those constituents of the blood which are requisite are selected, and combined to make the solid principles entering into the brain composition. One can conceive that this selective power seizes hold of a fat or similar principle, together with a suitable form of phosphoric acid, and also neurine, and these substances being thus more intimately brought in contact, they, through the synthetical influence residing in the protoplasm, combine, giving rise to those complicated substances with whose chemistry we shall elsewhere make ourselves familiar. Allowing that the larger number of principles met with in the living body are excretory; that is, products of analytical or destructive change, there yet remain a scarcely inferior number of other principles which, as they do not exist in our food, must be regarded as the products of synthesis or construction elaborated in the body itself.

The proper pursuit of chemical enquiry has taught us somewhat of these various processes and products, and will in its perpetuation yield much more—almost an unlimited amount of information.

It will be seen that the researches of chemists—such as those of Schützenberger—directed upon albuminous bodies, have thrown much light upon what may be called the excretory power in life, so that we may say with tolerable certainty, that this and that constituent of the urine have been derived from the decomposition of albumin. So in the future, as this sort of knowledge shall increase, we may possibly be able to trace back all excretory substances, not only to their parent molecules, but also to indicate the very processes which have led to their production.

Schützenberger's method of procedure was one employed beforehand by Strecker in many of his investigations, and is the same as that employed by Thudichum in his study of the constitution of brain principles. And this method is a proper method, because it is in imitation of that natural hydration process incessantly going on in the living body. But it has been shown that oxidation by air also occurs within the body, and hence it is reasonable to expect that researches having for their object the study of the mild oxidising power, or that united with one of hydration, as applied to albuminous and other principles, would lead to even more important information than any of which mankind is now in possession.

The blood may be viewed as a solution containing a variety of substances exposed to the action of dissolved and combined oxygen; a similar process is going on at every point of the body reached by the blood currents. Hydration is also going on here and there, if not everywhere, and the two processes often together. What wonder, then, that the multitude of substances thus elaborated and produced is so great. Even the substances thus elaborated and produced act and react, and thus the number is increased till it becomes almost endless. It is in the power of chemists to imitate such a state of things to some extent in the laboratory, but the power is one of which they have availed themselves as yet in a very small degree. Who can tell, for instance, what results might be obtained by studying the action of oxygen or air upon peptones, or upon the phosphorised matters of the brain, under conditions where hydration could not obtain, and also under other conditions where this process may precede or accompany that of oxidation? Such studies would probably throw much light upon the relations existing between bodies found in the blood, the brain, the bile, and the urine, and it is principally upon a perfected knowledge of such relations that we can hope for a philosophy of chemical physiology to be constructed. At present there is no such philosophy, but only a number of oases of facts, between some of which certain probable relations are dimly visible. But the connection is broken at almost every point, and thus we are left with a semi-rational view of life, and a less rational art of medicine.

PART II.

ORGANS, FLUIDS, AND PROCESSES CONCERNED IN DIGESTION, &c.

CHAPTER IV.

SALIVA AND ORAL DIGESTION.

BEFORE entering upon the study of foods and the nature of those best qualified to meet the demands of the system, it will be best to consider what those demands are, and the methods by which food is assimilated in the body.

Mixed Saliva and Oral Digestion.—The food is comminuted in the mouth by chewing, and at the same time it becomes mixed with the saliva—a mixture of fluids secreted by different salivary glands (the ducts of which discharge into the cavity of the mouth), and buccal mucus, or the secretion of the mucous membrane of the oral cavity, containing some few epithelial particles. Mixed human saliva is a turbid, opalescent, and somewhat viscid fluid, having a specific gravity of 1·004 to 1·006 generally; its specific gravity is very liable to variations, being dependent upon the amount of admixed mucus, and it not rarely rises as high as 1·025. According to Wright, saliva is denser after partaking of food than when observed under fasting conditions. It may be obtained in quantity by tickling the fauces with a feather. As thus obtained it presents a more or less alkaline reaction to test paper, and has the power of transforming starch into sugar, as first shown by Leuchs.

This power possessed by ptyalin, as the active principle of saliva is termed, resembles that of diastase, a ferment produced from malt, and one which Baron Liebig applied in the fabrication of a food for infants. Although we are unacquainted with the chemical identity of ptyaline, its action upon starch so far resembles that of many ferments and dilute sulphuric acid, in that it consists in determining the molecular addition of water to starch, thereby producing sugar,

$$C_6H_{10}O_5 + H_2O = C_6H_{12}O_6.$$

In a paper by Lefberg and Georgieski,[1] it has been shown that all starches are not affected alike. Thus potato-starch is converted more easily than wheaten starch, while maize-starch occupies an intermediate position; soluble starch behaves like potato-starch.

Starch, as is well known, consists of an outer coating of cellulose enclosing alternating layers of granulose, and although these bodies present the same empiric composition, there is a considerable difference of property betrayed by the two. Thus granulose is immediately coloured blue by iodine, whereas cellulose does not exhibit this reaction until it has been first exposed to the action of sulphuric acid or zinc chloride. Similarly, in the action of saliva upon starch it is the granulose which is first converted into dextrine and sugar, and only after some time, or at higher temperatures, is the cellulose likewise altered. Of these specific changes, however, we shall have more to say in another place.

Ptyalin may be isolated in a measure, though not in a pure state (probably), by precipitating fresh saliva with phosphate of lime produced *in situ*, that is, by the addition of phosphoric acid and lime water. In this way the ferment is carried down in a mechanical manner with the calcic phosphate, and may be afterwards extracted by water. From the aqueous solution it is precipitated by alcohol, and by continually repeating the solution in water and reprecipitation by alcohol, ptyalin is obtained in a snow-white form; its composition has not yet been determined. As it fails to give the xanthoproteic reaction with nitric acid, it is not regarded as an albuminoïd, although it is not improbably derived from some such substance. Its solution does not coagulate on heating, but its fermentive power is destroyed at 60°; it is also destroyed by strong acids and alkalies, and does not take place at 0°C. Ptyalin is most active at 40°C.

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[1] *Bull. Soc. Chim.* [2] xxv. 393.

Besides ptyalin, mixed saliva contains, as we have seen, mucus, a small quantity of undetermined fat or fatty acids, potassic and sodic sulphocyanides, calcium, and alkaline carbonates. According to R. Böttger,[1] he has obtained indications of the presence of a nitrite in saliva by acidifying with sulphuric acid, and adding a mixture of cadmium iodide and starch, when a blue colour is said to be produced.

The presence of sulphocyanogen in saliva is peculiar to man, and its function remains unexplained, although one author (Kletzinsky) has suggested that its presence resists the formation of fungi between the teeth. A tooth-brush would do this as well! Sulphocyanides are recognised in saliva by the red colour which ferric chloride imparts to it, or to the distillate obtained by boiling it with acids. This colour disappears on adding mercuric chloride, and thus distinguishes it from that given by meconic acid.

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[1] *Chem. Centr.* 1872, 741.

R. Böttger[1] recommends, in preference to this test, to impregnate a strip of Swedish filter paper with tincture of guaiacum, dry, and afterwards pass through a solution of cupric sulphate (1 in 2000); paper thus prepared instantly turns blue when moistened with saliva. Wright found the quantity of sulphocyanides to increase under medicinal treatment involving consumption of sulphur.

Calcium exists in combination in saliva other than as carbonate, perhaps with ptyalin, for if it be allowed to stand in the air, a crust of calcic carbonate forms over the surface; it is not improbable, however, that it exists as bicarbonate. The deposits of so-called tartar, which frequently are allowed to form upon the teeth, consist of calcic carbonate which is derived from saliva. Magnesium is also found in saliva, and traces of phosphoric acid, alkaline chlorides, carbonates, and sometimes sulphates, but their proportions, as also those of the other constituents, are by no means constant. Lehmann determined the fixed solids in mixed saliva at 0·388 to 0·841 per cent.; frequently, however, 1·5 per cent. is found. Ptyalin constitutes about one third of the soluble solids of saliva.

The following analysis of mixed saliva[2] exhibits its general composition

Water 994	Ptyalin	= 1·4
Solids 6	Mucus	= 1·5
= 1000	Fat	= 1·3
	Sulphocyanides	= 0·1
	Salts	= 1·7

Besides the previously enumerated constituents of saliva, albumin is invariably present in small quantity in the respective forms known as globulin and mucin. As hereafter we shall consider albuminous principles at some length, we need not refer more particularly to them in this place.

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[1] *Zeitschr. Anal. Chem.* xi. 350.

[2] Taken from Ralfe's *Physiological Chemistry*, where source is not stated.

The part taken by saliva in the great process of digestion is not thoroughly known, but there can be no doubt that one of the most important functions of saliva is exerted through the power of ptyalin to convert the starchy matters contained in food into sugar, as already described. It has been pretty well ascertained experimentally by Lehmann and others, that there is scarcely time for this process to complete itself in the mouth; it is continued in the stomach and the smaller intestine.

Saliva serves also to moisten the food, and thus it facilitates the act of deglutition; this is, of course, an important point, and from what we know, it appears to admit of experimental confirmation by the fact that dry foods cause a more abundant flow of saliva than wet foods or liquids.

Liebig suggested, from the frothy nature of saliva, and the fact that it occurs full of air bubbles, that one of its purposes was to convey air to the stomach and intestinal canal. All that can be said, however, in favour of this view is that it has not yet been determined whether the presence of air is essential to the transformation of starch into sugar by means of ptyalin; probably it is not.

The quantity of mixed saliva secreted by a man in 24 hours varies between 300 and 1500 grammes; it is increased by excitants and certain medicines and poisons.

Particular Salivary Secretions.—There are four kinds of salivary glands, and the secretion furnished by each of these is distinct in character.[1]

The sublingual gland lies underneath the tongue, while the submaxillary glands are situated on the sides of the tongue underneath the lower jaw; all these glands, however, discharge into the same duct, which lies underneath the forepart of the tongue. From these and the parotid glands the saliva is collected by the introduction of canulæ into the ducts, but the secretion of one and the same gland or set of glands may vary according to the agencies which call them into action. For these reasons and the difficulty attached to the operation of collecting saliva, the chemical nature of the secretions of distinct glands is but little known. Four different kinds of secretion, however, are recognised, according to the nerves whose irritation has furnished the supply.

Chordal saliva is secreted by the submaxillary glands on irritation of a nerve which is a branch of the facial, and is termed 'chorda tympani.' Its composition is described by Thudichum as follows:—

Solid matters = 4 per cent. {
= 1·5 Globulin, mucin, and coagulable albumin.
= 2·5 mainly alkaline chlorides and lime salts (chiefly bicarbonate).

Sympathetic saliva is furnished on irritation of the sympathetic nerve, and is collected from the submaxillary glands. It is opaque and tough in character, contains from 15 to 28 per mille of solids and much free alkali.

Ganglionic saliva flows when the submaxillary ganglion is made the centre of a reflex action working by way of the lingual nerve.

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[1] Lehmann's *Physiological Chemistry*, vol. ii. Also Thudichum's *Physiological Chemistry*.

Paralytic saliva is very thin, and contains but little solid matter; it results under the influence of nervous paralysis, caused by degeneration, or poisoning, or wounds which separate the secretory nerves. Nothing is known of its composition.

Parotid saliva is alkaline and viscous, and has the following composition in 1000 parts:—

Water	= 995·3
Organic matter—ptyalin, albumin, globulin	= 1·4
Calcium carbonate	= 1·2
Other mineral matters	= 2·1
	1000·0

Pathological Aspects of Saliva.—The presence of lactic acid in saliva has been frequently asserted, but while there is great doubt about it, it is certain that during some diseases the saliva grows more or less acid; thus, according to Donne,[1] saliva is acid in inflammatory affections of the primæ viæ, in pleuritis, encephalitis, &c., &c. Wright assumes the acid state sometimes observed in saliva to be referable to, among other diseases, rachitis. But all these and many similar observations are not worth much credit, being too vague, and admitting of no reduction to definiteness. It is also said that lactic acid is to be found in saliva in cases of diabetes, but the statement has as often been contradicted. In salivation produced by mercury, the sulphocyanides ordinarily present disappear from saliva, and mercury appears.

Many medicinal preparations, such as potassic iodide and chlorate, readily pass from the blood into the saliva, and may be detected there long before they appear in the urine. Leucine has been found in the paralytic saliva of hysteric persons, and in other diseases the presence of urea has been stated; this is not surprising, for in cases of cholera it appears in quantity in the brain also. According to Wright, biliary matters, and especially cholesterine, sometimes even pus, pass into the saliva, but Lehmann viewed Wright's work on saliva with considerable suspicion. Some of his work is, however, of no mean value; and, among other matters, he states that he was led by experiment to lend confirmation to the old opinion that the saliva of enraged animals, or men during violent anger, is capable of inducing suspiciously morbid symptoms when introduced into the blood. Later experiments by Lehmann and Jacubowitsch have not supported the results obtained by Wright, although, as is well known, saliva is the carrier of the contact ferment-poison by which hydrophobia is propagated.

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[1] *Histoire physiol. et pathol. de la Salive.* Paris, 1836.

CHAPTER V.

GASTRIC JUICE AND GASTRIC DIGESTION.

Résumé of Gastric Digestion.—The food, reduced to a pulp in the mouth and mixed with saliva and air-bubbles, arrives in the stomach and there undergoes what is termed gastric digestion. The mucous membrane lining the walls of the stomach is covered with multitudes of simple glands which open upon its surface, and among these there occur others which are more complicated, and have their blind ends subdivided. These latter are the *peptic glands*, which are excited by the presence of food in the stomach to excrete a thin acid fluid, called the gastric juice. The contractions of the stomach roll the food about and thoroughly incorporate it with this said juice, forming, in process of time, a matter of considerable consistency called chyme.

Description and Characters of Gastric Juice.—Gastric juice is an acid, glairy, slightly yellowish fluid of varying specific gravity, according to the means adopted for causing its flow and the relative time of collecting it to that when food was last in the stomach, &c. At early stages in the process of digestion it has a specific gravity of 1·010. It does not become turbid on boiling, and has no great tendency to putrefaction. Its composition, which is no doubt not a constant, has been variously given.

Thus Schmidt,[1] who made an analysis of a sample obtained from a woman suffering from gastric fistula, assigned to it the following constitution:—

Specific gravity		1·020
Water	=	954·13
Pepsin	=	0·78
Sugar, albuminates, lactic and butyric acids, ammonia, &c.	=	38·43
Potassic chloride	=	0·70
Sodic chloride	=	4·26
Potash	=	0·17
Calcic phosphate	=	1·03
Magnesic phosphate	=	0·47
Ferric phosphate	=	0·01

From the presence of sugar, albuminates, &c., it will be seen that this analysis refers to gastric juice mixed with food which has been to some extent previously altered by saliva. This probably explains why the fluid thus examined was slightly alkaline, a result which would be brought about by the presence of saliva. This is confirmed by the fact that when the gastric juice was made to flow by introducing peas into the stomach, it was obtained unmixed with saliva, and containing free hydrochloric acid.

The amount of gastric juice secreted daily by the human stomach has been variously estimated. Gruenewaldt[2] estimated it at 264 grms. for every kilogramme of body weight, or about 31 lbs. in twenty-four hours. Other determinations lead only to about 10 per cent. of the body weight, or 16 lbs.

Schmidt determined the amount of free hydrochloric acid in dogs' gastric juice at from 0·245 to 0·423 per cent., and also found traces of chloride of ammonium.

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[1] Lehmann's *Physiological Chemistry*, vol. 3, Appendix, p. 503.

[2] *Succi gastrici humani Indoles physica et chemica*, ed. Dorp. Liv. 1853.

L. Rabutem and F. Papillon[1] have demonstrated the presence of hydrochloric acid in the gastric juice of the ray, and a metallic bromide, but no hydrobromic acid.

Mr. Ralfe,[2] without naming the source of his analysis, gives the following composition to human gastric juice.

Specific gravity		1·0010
Water	=	975·00
Organic matter and pepsin	=	15·00
Free acid	=	4·78
Sodium chloride	=	1·70
Potassic "	=	1·08
Calcic "	=	0·20
Ammonic "	=	0·65
Calcic phosphate	=	1·48
Magnesic "	=	0·06
Ferric "	=	0·05

Thudichum expresses[3] the composition of this juice as follows :—

(1) Water	994·6
(2) Solid and permanently fluid ingredients, other than water	5·39
(3) Contains pepsine	3·0
Hydrochloric acid	0·2
Perhaps a little lactic acid.	
Chlorides of the alkalies.	
Phosphates of the earths.	

Ch. Richet, in some observations[4] upon digestion, made through the agency of a gastric fistula, points out that the mean acidity of the gastric juice, whether pure or mixed with food, is nearly equivalent to 1·7 grm. of hydrochloric acid per 1000 grms. of liquid. The highest acidity observed was 3·2 grms., and the lowest 0·5. It appears, also, according to this author, that the acidity is not influenced by the quantity of fluid in the stomach, but is invariable, or almost so, whether the stomach be empty or full. The acidity is increased by alcoholic drinks, but diminished by cane-sugar. When acid or alkaline liquids are injected into the stomach, the gastric juice reassumes its normal acidity in about one hour. The gastric juice is more acid during digestion, and the acidity increases with the digestion. M. Ch. Richet comes also to the conclusion that hunger does not result solely from emptiness of the stomach.

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[1] *Compt. Rend.* lxxvii. 135–138.

[2] Ralfe, *Physiological Chemistry*, p. 128.

[3] Thudichum, *Chemical Physiology*, p. 10.

[4] *Compt. Rend.* lxxxiv. 450, 452.

Before going further, it should be stated that inasmuch as the juice examined has been mainly obtained from persons suffering from fistulas, or from dogs upon whom fistulas have been produced by certain operations, it is difficult to say how far the analyses are to be regarded as representing normal gastric juice or morbid juice. These studies, however, led to the formation of what is termed artificial juice, and most of the properties possessed by gastric juice have been ascertained from a study of this preparation. We shall consider this matter further presently. For the moment, we may view gastric juice as a fluid containing dilute hydrochloric acid, and a ferment termed pepsin.

Function of Gastric Juice.—Together, these substances have the power of dissolving otherwise insoluble albuminous substances, such as white of egg, fibrin, casein, gristle, gluten, &c., thereby yielding thick turbid solutions of what are called peptones. Connective tissues are not so readily attacked by gastric juice, and fats do not appear to be altered by contact with it.

By being rendered soluble, the food henceforth becomes assimilable by the blood system, and the product, or chyme (a solution of peptones mixed with saliva and saccharine matter resulting from the action of saliva upon starchy matters) is, to some extent, absorbed by imbibition through the walls of numerous delicate vessels which convey it from the stomach to the blood, and thence to the vena portæ. This absorption is no doubt effected by a process of dialysis. These peptone solutions, unlike albumin in its ordinary forms, easily dialyse through parchment paper. Part, however, of the chyme escapes through the pylorus and enters the duodenum, where a distinct kind of digestive process is carried on. This will be considered in another chapter. Let us here consider more fully the nature of the constituents of gastric juice and their functions.

Nature of Pepsin.—Pepsin may be isolated by the same method described already for isolating ptyaline, viz., by its adhesion to phosphate of lime precipitated *in situ*.

It may be also prepared by macerating the mucous membrane of the stomach of a recently killed animal (rejecting the pylorus) in dilute phosphoric acid. It is in this way dissolved, and the solution, on precipitation with lime water, yields a precipitate from which the pepsin may be extracted by glycerine. Another method consists in the re-solution of the phosphate precipitate in very dilute hydrochloric acid and addition to this of a saturated solution of cholesterine, consisting of 1 part ether and 4 of alcohol. This latter is best added down a thistle funnel, and the whole mixture well agitated. The cholesterine thus separates, and as it rises to the surface it attaches the pepsin to itself in a mechanical manner. The cholesterine may be subsequently removed after filtration, by means of ether, and tolerably pure pepsin is thus left behind.

Although pepsin is a ferment evidently of albuminous origin, it is not ordinarily considered as a form of albumin, and mainly because it does not yield the xanthoprotein reaction (*see* Albumin) with nitric acid. In a subsequent place, however, it will be shown that it possesses undoubted relations to albuminous substances.

Pepsin is not itself destroyed during digestion, and thus far its functions appear to belong to what are termed 'contact actions;' that is to say, it is able to resolve large quantities of solids into a soluble form in the presence of dilute acids—more particularly at 40°. This action is well exhibited by exposing some pieces of coagulated white of egg to a faintly acid solution of pepsin; they are speedily and entirely dissolved. When, however, the liquor is saturated with peptones it ceases to act, just as yeast ceases to cause fermentation of sucrose solutions when the percentage of alcohol rises above a certain extent. An addition of acid fluid enables further digestion, however, to take place. As is well known, pepsin occurs now in various commercial forms, and is extracted chiefly from pigs' stomachs.

Pepsin may be obtained in the form of a greyish powder by precipitation; it is insoluble in alcohol and ether, but very soluble in dilute acids and glycerine. Its solutions are precipitated by alcohol, and coagulated by boiling; once boiled, its solutions lose their power of digesting, and the same ability is destroyed by a neutralisation of the acid solutions. Aqueous solutions of pepsin are precipitated by corrosive sublimate, by lead salts, and by solutions of tannic acid.

The Acid of Gastric Juice.—The nature of the acid in the gastric juice has been the subject of much dispute. Blondlot maintained that it consisted of phosphoric acid existing as acid phosphate of calcium. Others have regarded the acidity of gastric juice as due to the organic acids contained in or developed from the food by means of pepsin and ptyalin. Yet others have asserted the acidity referable to the presence of lactic acid, many investigators having again and again detailed the means whereby they have established the presence of that acid, and others denying this statement on experimental data with equal enthusiasm. The matter appears, therefore, to be still somewhat unsettled so far as the normal occurrence of lactic acid in gastric juice is concerned. This lactic acid has been supposed by some to be formed from carbohydrates by the action of ferments.

Lehmann and others state to have found lactic acid in gastric juice, while Schmidt and Maly failed in their attempts to identify it. One thing, however, has gradually become matter of certainty, that the main acidity of the gastric juice is due to free hydrochloric acid.

R. Maly[1] has recently made an investigation of the source of the acid of the gastric juice, the details of which are not without interest, confirming as they do in a singular manner the hypothesis first advanced by Thudichum, and described later on. Maly wished to find out whether the hydrochloric acid was derived from the dissociation of neutral chlorides or from their decomposition by lactic acid formed from carbohydrates. From a numerous series of experiments upon dogs, he arrived at the conclusion that the source of the free hydrochloric acid is to be sought in the dissociation of chlorides without the aid of an acid; and further, that the formation of lactic acid from carbohydrates is not a function of the living membrane of the stomach. Incidentally, several important facts were demonstrated; first, that chlorides of sodium distilled with lactic acid yielded traces only of hydrochloric acid towards the end of the operation; and, secondly, that when lactic acid was allowed to diffuse in presence of ferrous, sodium, calcium and magnesium chlorides, free hydrochloric acid was produced.

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[1] *Ann. Chem.*, clxxiii. 227–273.

In a series of experiments with the mucous membrane of pig's stomach, he found that at 40° with 2 per cent. solutions of grape-sugar, cane-sugar, milk-sugar, and dextrin, lactic acid was formed; but he views this result as due to the presence of a special organised body, and not a soluble chemical ferment. Interesting as these experiments are, they leave a margin for doubt, but we pass on to consider Thudichum's hypothesis above alluded to.

The Function of the Acid.—Thudichum [1] assumes that in the walls of the stomach, chloride and lactate of sodium are split up into the free acids and caustic soda; in this way the decomposition of salt would be represented thus, $NaCl + H_2O = NaHO + HCl$. But inasmuch as we never meet with caustic soda in the animal economy, at first blush the above idea would appear to be negatived. Thudichum, however, supposes that before the soda enters the blood it has a distinct function to perform, and that is the protection of the stomach against the corrosive action of its own excretion. Under certain abnormal conditions this corrosive action really obtains, and gives rise to gastric ulcer and other pathological processes. In the blood Thudichum supposes that the caustic soda is converted into carbonate, and passing through the gastric veins into the portal, enters the liver. There its function is completed, but its consideration must be left until we come to study bile and its influence upon the process of digestion.

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[1] *Chemical Physiology*, pp. 14 and 15.

General Characters of Chyme and Peptones.—As above stated, the product of stomachic digestion is chyme, containing starch, sugar, fat, and peptones (if both carbohydrates and animal matters have been eaten). It appears also that there are present a number (five or more) of albuminous substances more or less closely related on the one hand to peptones, strictly speaking, and on the other hand to unaltered albumin. It is probable that these but represent the various phases presented in the gradual change of ordinary albumin under the influence of hydrochloric acid and pepsin.

The peptones, curiously enough, mainly agree in general composition with the original matters from which they are produced, a result which shows that the change is more of an intermolecular nature than a splitting-up. Peptone solutions are not coagulated by boiling, but are precipitated by absolute alcohol. With nitrate and nitrite of mercury they give Millon's reaction; optically, they turn the plane of polarisation towards the left.

The Specific Nature and Actions of Pepsin.—Liebig showed many years ago that if albuminous matters were so exposed to air and moisture as to undergo partial putrefaction, even if to a very slight extent, the whole would liquify and become a diffusible fluid of a composition agreeing with that of the original unchanged matter. That is to say, in the change of a minute fraction some sort of ferment or agent is generated which has the power of acting upon the remaining quantity as pepsin acts on albumin. Moreover, Liebig said what we call pepsin is but a part of a mucous membrane which in its own particular composition is identical with those albuminous principles whose properties are changed by contact with it; in fact, said he, the tendency to change inherent in the living tissue is communicated by contact to those similar but non-living matters outside. In the present day science has no better explanation than this to offer.

In another place we give an account of some researches of Alex. Schmidt and of Erlenmeyer, which, taken in conjunction with the work of Schützenberger, promise to throw much light upon the general nature of chemical ferments in the human body, and their relation to that form of matter ordinarily called albumin.

Abnormal Constituents of Gastric Juice.—Very little is known regarding the pathological phases of gastric juice. In cases of gastric catarrh the mucus of the stomach appears to accumulate to an abnormal extent, and to induce processes which result in the formation of acetic, butyric, and lactic acids, thus increasing the normal acidity of the stomach. In uræmia, or after extirpation of the kidneys, urea is said to be secreted by the gastric glands.

CHAPTER VI.

THE BILE; PANCREATIC, INTESTINAL, AND SPLENETIC JUICES; INTESTINAL DIGESTION AND FÆCES.

It has been shown in the last chapter, that while yet in the stomach a certain quantity of the chyme undergoes direct absorption into the blood system. Another part, however, passes through a further process called duodenal digestion, where bile and pancreatic juice play a prominent part. Before proceeding to the study of this and intestinal digestion, it is proposed to make ourselves acquainted with the general nature and properties of these fluids, beginning with the bile. Among the functions of the liver the most important is its secretion of bile; it has other functions, whose study, however, is best postponed for a time.

General Characters of Bile.—Bile is one of the most complicated secretions of the human body, and has a most important chemistry. It accumulates probably continuously, but is expelled during digestion from the gall-bladder wherein it is stored, and a further quantity escapes during the emptying of the stomach. As taken from the gall-bladder, it often receives the name of gall or cystic bile; and when warm smells like musk. It constitutes a viscid liquid of a yellowish-green colour, but which becomes strongly yellow on dilution; it is heavier than water (sp. gr. 1·02), and owes its viscidity to the presence of a quantity of mucus derived from the gall-bladder. Until this mucus be removed, bile exhibits a tendency to undergo putrefactive change, but if the mucus be removed by dilution, addition of acetic acid (thereby producing coagulation), and filtration, it is readily preserved. Human bile has been studied, but not so intimately as ox bile, the former being obtained only from fistulous openings, whereas there is no difficulty in obtaining that from the ox; this is of a green colour.

The following analysis given by Berzelius[1] is useful as representing, in a general way only, the composition of ox-bile.

Water	90·44
Biliary and fatty bodies	8·00
Mucus	0·30
Watery extract, chlorides, phosphates, and lactates	0·48
Soda	0·41

The composition presented by the bile of various animals has been shown by Strecker[2] to differ only in the varying proportions in which two of its constituents (taurocholic and glycocholic acids) exist therein. Thus he has stated that the bile of the dog is almost free from the sodium salt of glycocholic acid, without regard to the nature of the food; while the bile of the sheep, and that of the goose (Marsson), contains chiefly taurocholate of sodium also. The bile of the pig is characterised by hyocholic acid.

Somewhat different estimates have been given of the amount of bile secreted in the human body, one fixing it at 1200 grms. per day, while others give varying quantities from about 30 to 800 grms. per 24 hours. Bile appears to be most actively secreted shortly after eating, when the solids constitute about 5 per cent.; these increase up to about 10 per cent., and then decrease again to 5 per cent. during fasting. The quantity secreted by each animal seems to be peculiar, and not to bear any definite relation either to the body weight, or, as Thudichum suggests, to the size and weight of the liver, but rather to the size and weight of the liver in relation to the weight of the blood, since, as we shall hereafter see, it is from this fluid that the liver elaborates the bile.

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[1] Miller's *Chemistry*, Part iii. [1867] p. 883.

[2] *Ann. de Chem. und Pharm.*, Bd. 70, S. 149–198.

It is a curious fact that most of the salts found in the bile of salt-water fishes have potassium as their base, while the bile of fresh-water fishes contains chiefly sodium salts.

Most of the literature relating to the chemistry of the bile is without value; Strecker's researches stand out, however, from the others before and since in a remarkable manner, and it is to his work that we owe most of our knowledge regarding its composition. Bile, then, contains taurocholate and glycocholate of sodium (resinoid salts), and a number of colouring matters, the chief of which are bilirubin and bilifuscine; a third colouring principle is termed biliprasine. Bile also contains lecithine, choline, and cholesterine, but is free from albumin. Ox bile is also said to contain a small amount of stearic, oleic, and lactic acids, in combination with potassium and ammonium. As bilirubin occurs in bile, it appears to exist as lime salt, the brown granules of which may often be observed while examining bile microscopically. Phosphates of sodium, calcium, and iron, sodic chloride and traces of copper, are also contained in bile.

O. Jacobsen,[1] in an analysis of the ash of bile obtained from an abscess, found the following quantities in 100 parts of dog bile—

KCl	1·276
NaCl	24·508
Na_2CO_3	4·180
Na_3PO_4	5·984
$Ca_3(PO_4)_2$	1·672

C. G. Lehmann[2] claims to have demonstrated the presence of preformed alkaline carbonates in ox bile. Thus in one experiment he found 0·0046 per cent., and in a second 0·1124 per cent., normal sodic carbonate. This fact has a very important bearing upon our views of the great process of digestion, and is particularly instructive when viewed in connection with Thudichum's hypothesis regarding gastric digestion.

Biliary concretions, when they occur in man, consist of cholesterine, colouring matters, earthy salts, and other principles not so well ascertained. Corresponding concretions are liable to occur also in other animals.

THE PANCREAS AND THE PANCREATIC JUICE.

The pancreas is constructed in the main of albuminous substances, but it contains also a considerable quantity of leucine, xanthine, hypoxanthine, and guanine. The ferments, to which further allusion will be made under pancreatic juice, may be extracted from it by suitable means.

The function of its secretion is entirely confined to the digestive processes. Its nature has been studied upon the juice obtained from temporary or permanent fistulas, while the properties of the ferments contained in it have been ascertained by isolating them in an impure form from the pancreas itself.

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[1] *Deut. Chem. Ges. Ber*, vi. 1026–1029.

[2] Lehmann's *Phys. Chem.*, vol. ii. p. 67. English Translation.

General Characters of Pancreatic Juice.—Pancreatic juice is a more or less tough, viscid secretion of alkaline reaction, and having a specific gravity of from 1·008 to 1·009, or somewhat greater. It contains from 10 to 11 per cent. of solids, and is peculiarly liable to putrefactive change after removal from the body. According to Ralfe's 'Physiological Chemistry,' its composition is as follows:—

Water	900·76
Organic matter	90·38
Sodium chloride	7·36
Free alkali	0·32
Sodium phosphate	0·45
" sulphate	0·10
Potassium "	0·02
Combinations of lime	0·54
" magnesium	0·05
" iron	0·02

The organic matter of pancreatic juice contains soluble albumin and alkali-albuminate, ferment matters, and often small quantities of fat, leucine, tyrosin, butyric acid, &c.

According to Gmelin and Tiedemann, it sometimes contains as much as 4 per cent. soluble albumin, and it is not unlikely that this exists as an intermediate formation to be afterwards elaborated into ferment matters, or which has resulted from the action of the ferments upon fibrin. Kühne states that the prolonged action of pancreatic ferments upon peptones leads to the formation of leucine and tyrosin; and, as we shall see in a future chapter, these bodies are known to result from a certain decomposition of albumin. Basil Kistiakowsky[1] has also observed that by the action of pancreatic juice on fibrin, leucine, tyrosin, and glutamic acid result. S. Radziejewski and E. Salskowski,[2] in the same process, have observed, moreover, the production of aspartic acid (viz., by digestion of fibrine at 40–50°).

Although from time to time statements have been made relative to the isolation of the pancreatic ferments, yet so far as can be judged, they have never been isolated as chemical individuals, but always in a form associated more or less with foreign matters. Some writers speak of the existence of three ferments in pancreatic juice, and Danilewsky has affirmed that he has separated two of these.

Such preparations are obtained by various methods, the best of which is that recommended by Wittich, which consists in reducing the pancreas of the ox to a mincemeat, hardening by standing in alcohol for 24 hours, and extraction by glycerine. From the filtered extract, alcohol precipitates the ferment-matter. In a more impure form it may be isolated also by rubbing down ox pancreas with sand or broken glass, extraction with water, and precipitation of the extract with alcohol.

Of the amount of pancreatic juice secreted, many various estimates have been made, but little reliance can be placed upon them, since the observations have been effected under more or less deranged physiological conditions. From certain experiments upon dogs, Bidder and Schmidt have calculated that an adult man, weighing 10 stone, secretes 150 grammes in 24 hours.

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[1] Pflüger's *Archiv. für Physiologie*, ix. 438–459.

[2] *Deut. Chem. Ges. Ber.*, vii. 1050–1051.

According to Frerichs, it is only secreted during digestion.

The pancreatic juice appears to exercise a number of functions, which may be expressed as follows:—

(a) The completion of the solution of imperfectly digested matters issuing with the chyme from the stomach; so-called albuminoïds being converted into albuminones, or substances soluble in alcohol and not coagulable by heat.

(b) The emulging of neutral fats. Pancreatic juice makes perfect emulsions when agitated with neutral oils, and it was chiefly upon observations of this kind, backed up by certain physiological experiments, that Bernard came to the conclusion that one of the chief functions of pancreatic juice is to aid in the assimilation of fatty substances. Bidder and Schmidt and others, however, in more recent experiments, gave no support to these views.

The emulsion of neutral fat transforms it into such a fine state of subdivision that it can pass through the pores of the mucous membranes into the chyle ducts.

(c) Pancreatic juice is further supposed to have the power of splitting up neutral fats into free fatty acids and glycerine, and it appears certain that among other products of the decomposition of fatty matters, butyric acid has been well recognised.

(d) It has also the property, in an intense degree, of converting starch into sugar, thus completing any change of this kind that may have been left unfinished by the saliva in the mouth and stomach.

One of the few attempts that have been made to obtain precise chemical information regarding the changes undergone by albuminöid under the influences of pancreatic ferments, is by Basil Kistiakowsky (see his paper above referred to). He obtained pancreatic ferment matter by Wittich's process, and then investigated its action upon fibrin (from ox blood) by digesting the latter in an aqueous solution of the ferment during a number of hours. The original fibrin was not pure, yielding 0·625 per cent. ash, and on analysis it yielded numbers approximating to the formula $C_{139}H_{226}N_{37}S\ O_{46}$. The peptone produced in the experiments described was also impure, yielding 1·186 per cent. ash, and on analysis it gave the composition $C_{113}H_{228}N_{36}S\ O_{66}$. Although these numbers and formulæ can only be regarded as approximately correct, yet this fact comes out, that the peptone contains less carbon and more oxygen than the original fibrin—a fact which may be related to the production of tyrosin, leucine, and similar bodies.

A failure in the supply of pancreatic juice has been viewed as the acting cause of certain diseases in which undigested lumps of fat are stated to pass out with the fæces. In lientery, also, the pancreas appears to be affected.

INTESTINAL JUICE.

General Character of Intestinal Juice.—But very little is known either of the constitution or the functions of intestinal juice, although there can be small doubt that its influence upon the great process of digestion is by no means unimportant.

From Frerichs's researches it would appear that Peyer's glands contribute but slightly to the formation of intestinal juice, while on the other hand, Brunner's glands and Lieberkühn's follicles are chiefly instrumental in its secretion.

From what is known (and that is next to nothing), it would seem that in chemical composition the fluids secreted in the small and large intestines are identical. According to the researches of Lehmann, Bidder and Schmidt, and Frerichs, intestinal juice is a yellowish viscid, transparent, alkaline secretion, which coagulates on treatment with chlorides and sulphates of the alkalies. It has a specific gravity of about 1·01, and contains from 2 to 2·5 per cent. solids, part of which is of a fatty nature.

While Thierry and Frerichs have not succeeded in establishing the fact of any important change of food through the influence of intestinal juice, Bidder and Schmidt concluded that it behaves very much in the same manner as does pancreatic juice. These last-named observers calculated (on grounds not sufficiently precise or reliable, however, for absolute acceptance) that an adult man, weighing 10 stone, secretes about 300 grms. of intestinal juice in twenty-four hours. Intestinal juice would seem to combine in itself to some extent the powers both of the gastric and pancreatic fluids, for while bile and pancreatic juice interfere with the digestion of albuminous matters by gastric juice, such is not the case when albuminoïds are in process of digestion by means of intestinal juice.

It is in the small intestine, apparently, that certain diseased processes have their origin, such, for instance, as cholera, typhus, and typhoid fever, &c.

THE SPLEEN AND ITS JUICE.

From a histological investigation of the spleen, Kölliker advanced the opinion that this organ was the seat of the solution and complete disintegration of the blood corpuscles, while it had been previously held that this organ was the seat of their formation. The opinion of Kölliker derived some support from a further study made by Ecker, but more especially from the researches of Scherer. This latter observer found in the splenic juice many characteristic decomposition products of the albuminous and other nitrogenous matters said to include the blood pigment itself. It was hence conjectured that the spleen accomplishes the destruction of those corpuscles which are no longer able to carry out their original functions. Among other acids of the same series, Scherer detected formic acid in the splenic juice, and also in leucæmic blood. It cannot, however, be said even now that we are properly acquainted with the functions of the spleen, although later researches make it more probable that it is connected rather with the construction of certain constituents of the blood and with the processes of digestion.

According to Thudichum[1] the spleen contains much blood, and hence it is difficult to procure its own juice in an unmixed state. The fresh spleen shows an alkaline reaction, but this becomes acid on standing. A water extract of the spleen contains hæmatocrystalline, albuminous matters, cholesterine, hypoxanthine, xanthine, and uric, lactic, succinic, formic, acetic, and butyric acids, leucin, and inosite.

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[1] *Chemical Physiology* (Longmans & Co.), p. 40.

Professor Schiff has recently published an important paper[1] upon the functions of the spleen, in which he shows that extirpation of this organ has no durable influence on the absolute or relative quantity of the white or red corpuscles of the blood. During stomachic digestion the spleen prepares the ferment which, entering with the blood into the tissue of the pancreas, transforms in this gland an albuminoïd substance into pancreatopepsin or trypsin, or, in other words, into a substance capable of digesting albuminous foods. After removal of the spleen the pancreatic juice loses its digestive influence upon such special substances, but otherwise retains its digestive properties. Although it is therefore evident from Schiff's and other researches that the spleen is actively employed in life, it yet appears that animals from which it has been removed by operation continue to live without any great disturbance.

Thudichum points out that in leucocythæmia the spleen is frequently large, and weighs from nine to ten pounds; when in that disease it is small, the lymphatic glands are always enlarged. Among diseases which affect the spleen one is particularly remarkable, namely, waxy or so-called amyloid degeneration. In such cases the spleen is indigestible in artificial gastric juice, and is not prone to change. Thudichum objects to the term 'amyloid' degeneration because the spleen in such disease gives no sugar on boiling with dilute sulphuric acid, which it would do if it contained any amyloid (starch-like) principle.

M. G. Pouchet, in a recent communication to the

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[1] Read before the Medical Congress of Geneva, 1877. *Gaz. Hebdomadaire*, Sept. 21, 1877.

Société de Biologie, has shown that in certain Selachian fishes the elements of the splenic parenchyma are undistinguishable from certain corpuscular elements contained in the blood, and hence he conjectures, in opposition to some views above stated, that the spleen is concerned in the genesis of the blood corpuscles. That the corpuscular elements in the blood of the fishes alluded to ultimately become transformed into red corpuscles appears beyond doubt, but M. G. Pouchet does not seem to have established this to be true of the splenic elements resembling them.

INTESTINAL DIGESTION.

After the completion of gastric digestion which has been already described, the chyme passes by way of the pylorus into the duodenum, and here the bile and pancreatic juice come into play; they flow through a common aperture, and convert chyme into chyle. We have seen (in the chapter on gastric digestion) that the soda set free by the action of the stomach walls upon sodic chloride ultimately reaches the liver and combines with carbonic and certain biliary acids, forming sodium salts therewith. Now the first action of the bile, as it mixes with the chyme, consists in the decomposition of these same sodium salts by the free acid of the gastric juice, and this is attended consequently with the formation, but not the precipitation, of free biliary acids.

Although Marcet held that the neutral fats are split up into free fatty acid and glycerine while yet in the stomach, no adequate evidence of such a change is forthcoming. Indeed we may view the action of bile and pancreatic juice (both of which are alkaline) to be one of saponification, the chyme assuming, after admixture with these juices, the form of an emulsion. In this way the fat is rendered absorbable by being enabled to pass through the fine pores of the mucous membranes, ultimately reaching the blood system.

While treating of this subject it is convenient to draw attention to the power of ordinary phosphate of sodium to emulsify certain fatty acids, and it is to the presence of this substance in bile that Thudichum (see his 'Chemical Physiology') attributes its property of emulsification.

In the duodenum the bile also causes a precipitation of peptones, and these being passed down the intestines with biliary acids and colouring matters, are altered and absorbed by the digestive influence of intestinal juice.

It is supposed that in the intestines the biliary acids split up, yielding taurine and glycocin, which return into the circulation, but the cholic acid (their complementary product) disappears for the most part. It is true a certain part of it occurs in the fæces, but this by no means accounts for the whole quantity, and it is not improbable that a large proportion of it is likewise absorbed into the system.

The pancreatic and intestinal juices also complete the transformation of the starchy matters present in chyme into glucose, and so, in one way or the other, the food introduced into the alimentary canal is rendered soluble and absorbable so far as this is possible.

The destiny of the biliary colouring matters is unknown, beyond the observation which has been made, that they are profoundly changed.

By means of the peristaltic contractions, the chyle is thrust along the small intestine, and the vessels of the villi absorb the dissolved matter, and admit of the passage of the minutely divided particles of fatty matter. At the same time much of the chyle enters the lacteals, and only reaches the blood system after travelling along the mesenteric lymphatics and the thoracic duct.

Passing through the ileo-cæcal valve, the digested matters enter the cæcum and the large intestine, and by this time they constitute a more consistent mass, owing to the removal of soluble and liquid matters. What remains is the insoluble residue of the food, and changed principles which have been of influence in its digestion.

It is in the large intestine that the excrementitious matters assume an acid reaction and peculiar odour, both of which features become more marked as they approach the rectum. It has been supposed that the acid reaction alluded to is owing to processes of fermentation arising in starchy matter which has escaped conversion into glucose, but the grounds on which this statement rests are far from satisfactory.

THE FÆCES.

General Description of Fæces.—Fæces represents the undigested and altered portions of the food which have refused absorption; its quantity and composition therefore necessarily vary with the nature and amount of the food. It contains certain changed products derived from biliary matters and the juices involved in digestion.

The fæces often have an acid reaction, which has been ascribed to the presence of lactic and butyric acids, though more often they are quite neutral and sometimes alkaline; as for the colour, this depends largely upon the nature of the diet, a flesh diet imparting a dark colour, while much milk causes them to be yellow. This last fact is probably connected with the observation of Thudichum, that the fæces of children at the breast contain a yellow matter, soluble in alcohol, and exhibiting an absorption band in its spectrum at the beginning of blue. Thudichum names this unknown substance 'intestino-luteine.' The fæces are more solid, and of a paler colour, when a bread diet is more resorted to. Many chemical reagents taken as medicines have an influence upon the colour of the fæces; thus it is well known that iron preparations give a black colour to the fæces, while mercurial ones lend a green colour.

Composition of Fæces.—Beyond the normal constituents of fæces, many extraordinary ones are liable to be found present, and depend also upon the nature of the food, &c. In illustration of this it may be stated that, in conjunction with Paul, the author has recently shown,[1] that when the diet includes preserved peas containing copper, this substance is excreted for the most part in the fæces. The copper exists in the form of an insoluble combination with the substance of the peas (albumin), and to a great extent resists digestion.

E. Vogt[2] found weighable quantities of morphine in the fæces of a man who had taken large quantities over a period of some years.

Unchanged bile is never met with in fæces, and Schmidt has shown that one half of the bile effused into the intestinal canal is decomposed before it reaches the middle of even the small intestine. Several products, however, derived from bile are to be found in the fæces, as will be hereafter shown. Meconium, or the matter found in the intestinal canal at birth, consists for the most part of biliary matters. Here it should be stated that Pettenkofer's test for bile is by no means reliable, and the explanation of this is given in a special chapter.

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[1] *Pharm. Journ.* September 1877.

[2] *Arch. Pharm.* (3), vii 23, 26.

At times certain matters are recognised to be present in fæces which admit of digestion and assimilation; therefore, when these occur they must be regarded not as excrementitious matters in the proper sense of the term, but as materials which have escaped, from some extraordinary circumstances, the action of the stomachic and the various digestive influences. Such a state of things often indicates conditions of disease.

As regards the odour of fæces, it in no way indicates any process of a putrefactive kind, but is merely a property of certain matters which are present, and which may otherwise be produced, as, for instance, by the action of alkalies (when fused) upon such bodies as casein, gelatin, and fibrin (Liebig). When out of the body, however, Liebig has shown that fæces are liable to putrefactive change, and have then the power to communicate a state of fermentation to other substances, such as sugar solutions.

The amount of water present in fæces is not a fixed quantity, but averages about 73 to 75 per cent.; it also contains about 26 per cent. matter, dry at 100°C., but this is the average of quantities ranging from 17 to 31 per cent. Fæces contains but little nitrogen; Dr. Edward Smith has stated that on the average the daily elimination of nitrogen by the bowels amounts to about 3 grms.

Liebig calculates that a healthy adult excretes about

5¼ ounces of fæces in twenty-four hours, but it is a varying quantity, and as often amounts to 7 or 8 ounces.

Mucus is present to the extent of a few per cents., and it is by no means improbable that the liability of fæces to putrefaction exhibited after removal from the body resides in this substance, which is known to be remarkably prone to such decomposition.

Fæces generally contains but small quantities of salts, consisting of phosphates of calcium, magnesium, sodium, and potassium; traces of iron are also present, and sometimes crystals of the ammonia-phosphate of magnesium. Chlorine and sulphuric acid occur only in traces.

Small quantities of albumin in a soluble form, and fats are also often met with, as well as glucose. This last-named substance is supposed to result from the action of pancreatic juice upon starchy matter in the intestine. Among the altered biliary matters excreted in the fæces there occur dyslysin, cholalic acid, choloidinic acid, taurin, and other perfectly undefinable substances chiefly derived from the biliary colouring matters. The undigested matters present in fæces include fat of a waxy and partly unknown nature, starch granules, cellular and muscular fibres, cellulose, particles of bone, &c., &c.

Gases are often occluded in the intestine, and more especially in cases of imperfect digestion; they consist for the most part of carbonic anhydride, with variable quantities of marsh gas (CH_4) and hydrosulphuric acid (H_2S). These symptoms are often painfully increased in disease; thus, in typhus fever, the stomach is often found distended with gas.

Some years ago Marcet submitted fæces to an elaborate investigation which was attended by a number of interesting results, the chief of which was the discovery of a new organic substance of an alkaline reaction, and which he named excretin. It is very soluble in ether, but sparingly soluble in cold alcohol; insoluble in water and crystallising in acicular forms. It fuses between 95° and 96° C., and burns away at higher temperatures leaving no ash. Ultimately, Marcet gave to this substance the formula $C_{78}H_{156}SO_2$. More recently F. Hinterberger[1] has re-investigated the matter, and found that Marcet's excretin was a mixture, the pure substance being free from sulphur and consisting of $C_{20}H_{36}O$. It is obtained by exhausting fresh fæces with boiling alcohol, and allowing the extracts to stand over a week, filtering from the black precipitate which forms, and precipitation with milk of lime. The precipitate thus obtained, after drying, yields the pure excretion to a hot mixture of ether and alcohol, and on cooling the extract below 0°, it deposits in the form of yellow needles. A hundred pounds of fæces yielded 8 grams of the pure material, which forms, with bromine, a crystalline substitution product of the formula $C_{20}H_{34}Br_2O$.

Marcet also examined the deposit thrown down on standing from the alcoholic extract of fresh fæces, and describes it as a soft fatty body which he named excretolic acid. This fuses between 25° and 26° C., and is not saponifiable by boiling potash. It is soluble in ether, but insoluble in water. It has never been analysed.

Stercorin is the name given by Dr. Flint to a substance which he found in fæces, and which he considers to be derived from cholesterine. It has not been analysed, but from its described characters it appears to be related in some way to, and is perhaps identical with, excretin or excretolic acid.

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[1] *Ann. Chem. Pharm.*, clxvi. 213-216.

Playfair found, in a sample of fæces which he examined, as much as 15 per cent. of nitrogen and 45 per cent. carbon, and from the amount of nitrogen and phosphates present, human fæces has often been recommended as a useful manure. Various plans for dealing with it have been from time to time discussed at the Society of Arts in London and elsewhere. Quite recently, H. Schwarz has proposed[1] a process which consists in heating human excrements with milk of lime, condensing the ammonia which is evolved, and separating and pressing the lime mud which is obtained; it is this mud which is recommended as a manure, but it appears to be of small value.

Fæces in Disease.—In the mucous evacuations from a case of intestinal catarrh, Liebig detected the presence of alloxan, an oxidation product of uric acid. Under abnormal conditions, uric acid, urea, leucine, &c., have also been observed present. These are facts which possess some sort of connection with the great process of oxidation which is constantly going on in the body, but the nature of the relation is quite unknown.

In cholera and typhus it has been stated that the serous evacuations contain much soluble albumin. Thudichum has examined cholera evacuations, and has incorporated the results in a report[2] on cholera.

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[1] *Dingl. polyt. J.*, ccxx. 161–171.

[2] *Reports of the Medical Officer of the Privy Council, &c.*

CHAPTER VII.

CHEMISTRY OF THE BILE.

IT is not intended in this place to discuss the function of the liver; that will come hereafter. Here it will suffice to state that beyond all doubt, the great purpose served by the liver is the production of bile, which it elaborates by unknown processes out of the matters contained in the blood which feeds it.

The general characters of bile have been already described; it is now necessary to study the chemistry, so far as it is known, of those constituents of bile with which we are acquainted. These may be said to be glycocholic and taurocholic acids (which exist as sodium salts), cholesterine, and the various biliary pigments.

Glycocholic acid, $C_{26}H_{43}NO_6$.—This acid constitutes the greater part of the resin of ox bile, but it is only present in small quantity in human bile. It is best obtained by fully extracting dry bile with absolute alcohol, and fractional precipitation of the extract with ether. The first precipitates consist for the most part of colouring matters; the latter ones are crystalline, and contain the sodium salts of glycocholic and taurocholic acids. The mixture last named is dissolved in water and precipitated by acetate of lead, when taurocholate of lead remains for the most part in solution. On decomposition of the lead glycocholate dissolved in hot alcohol, with sulphuretted hydrogen, the free acid is obtained, and is deposited as a white crystalline mass from the filtrate after removal of the sulphide of lead.

It is obtained in a purer state if the bile be first decolorised by animal charcoal, and it then only requires washing with water to be quite pure.

Gorup Besanez recommends the extraction of dry bile with alcohol of 90 per cent.; distillation of the excess of alcohol; dilution of the residual extract with water, and precipitation with milk of lime. In this way most of the colouring matter is thrown down in combination with the lime, and on neutralisation to faint acidity with sulphuric acid, the filtrate gradually deposits crystals of glycocholic acid.

Glycocholic acid forms long silky needles, which lose weight at 100° C; it is sparingly soluble in cold water, but dissolves freely in hot water. Recrystallisation from water may therefore be resorted to as method of purification. It is sparingly soluble in ether.

The salts which it forms with the metals of the alkalies and earths are crystalline, and are soluble in alcohol. Its aqueous solution is not precipitated by neutral lead acetate, mercuric chloride, or nitrate of silver, but the lead, copper, iron, and silver salts may be obtained by precipitation from its sodium salt held in solution.

The sodium salt will not crystallise from water or alcohol, but dries up to a varnish; it exists in this form naturally in bile.

The soluble glycocholates are decomposed by acetic and other acids, with the precipitation of glycocholic acid in a viscid form.

When glycocholic acid is boiled with a solution of baryta water, it is decomposed as follows:—

$$C_{26}H_{43}NO_6 + BaH_2O_2 = Ba(C_{24}H_{39}O_5)_2 + 2C_2H_5NO_2.$$

That is to say, the barium salt of cholic acid, and glycocine are produced.

Acids decompose it in a somewhat different manner; a molecule of water is first removed, and cholonic acid, $C_{26}H_{41}NO_5$, is produced; this then decomposes into choloidic acid, $C_{48}H_{78}O_9$, and glycocine; finally the choloidic acid is resolved into dyslysin, $C_{48}H_{72}O_6$.

It is not at all unlikely that the dyslysin and other allied compounds, the presence of which has been remarked in the fæces, results from a similar decomposition instituted by the acid of the gastric juice under conditions governing intestinal digestion. In that case glycocine would probably be reabsorbed into the system, and this view derives considerable support from some facts now to be mentioned. Hippuric acid, $C_9H_9NO_3$, is not a normal constituent of human urine, but is found in that of the horse and cow. But when benzoic acid is being taken, hippuric acid is found in the human secretion, and, curiously enough, hippuric acid readily decomposes by the agency of acids, as follows:—

$$C_9H_9NO_3 + H_2O = C_7H_6O_2 + C_2H_5NO_2.$$

That is to say, it splits up into benzoic acid and glycocine, suggesting the probability that the hippuric acid, when found in man's urine, has resulted from a synthesis of these substances by the removal of one molecule of water. It will be seen in another place that glycocine also bears a decided relation to many other bodies found in urine.

Taurocholic Acid, $C_{26}H_{45}NSO_7$.—This constituent of bile, which is peculiarly characterised by the sulphur it contains, is less abundant in ox bile than the corresponding acid. In the human bile, however, the order of things is reversed, and taurocholic acid is the most abundant (in dogs it is the only one).

It is prepared from the mother liquor resulting after the precipitation of the glycocholate of lead. As taurocholic acid is only precipitated by basic lead acetate, ammonia and more acetate of lead must be added to the mother liquor referred to. The precipitate is purified by dissolving in alcohol and reprecipitating by water, after which the alcoholic solution is decomposed with sulphuretted hydrogen, the sulphide of lead is removed, and the solution concentrated. The free acid may be obtained on evaporation, or by precipitation with ether, when it is deposited as a syrup which crystallises on continued standing.

Heintz recommends the direct precipitation of bile with normal lead acetate, and the precipitation of the filtrate with basic lead acetate, until the precipitates are white and of a plaster-like consistence. The ultimate filtrate yields nearly pure taurocholate of lead, if now precipitated with a mixture of basic lead acetate and ammonia.

The combinations of taurocholic acid with the alkali metals are very soluble in water and alcohol; the basic lead salt is soluble only in boiling water.

When decomposed by boiling with acids, it splits up much in the same way as glycocholic acid, yielding cholic or choloidic acids, or dyslysin; glycocine (glycocoll), however, it does not yield, but in its place taurin appears—

$$C_{26}H_{45}NSO_7 + H_2O = C_2H_7NSO_3 + C_{24}H_{40}O_5.$$

Baryta water, when boiled with taurocholic acid, also decomposes it, giving cholate of barium and taurin.

This same decomposition would appear to take place in the small intestine, taurin being found in the intestinal canal to some extent; most of it, however, gets into the circulation, and the sulphur it contains, representing the whole of that contained in bile, is excreted in the urine as sulphuric acid.

Cholic Acid ($C_{20}H_{40}O_5$).—This acid may be obtained as already described under taurocholic and glycocholic acids. Although it is probably produced as a decomposition product in the body, it is nowhere met with, and hence it would appear to become burnt up in the circulation.

It crystallises from alcohol in colourless glassy forms, but as obtained from its barium salt by decomposition with hydrochloric acid, it forms a resinous mass. Cholic acid is slightly soluble in water, more so in ether, and still more in hot alcohol. Its ethereal solution deposits the acid in rhombic tabular crystals, which contain one molecule of water of crystallisation which may be expelled at a gentle heat. At a higher temperature it loses water of constitution, and successively becomes choloidic acid and dyslysin.

The potassium, sodium, and barium cholates are soluble in water and in alcohol, and from the latter menstruum most of the salts crystallise, although in many characters they approach to the nature of soaps.

On oxidation with nitric acid, cholic acid yields cholesteric acid ($C_8H_{10}O_5$).

Cholic acid fuses at 195° C., and crystallises with 2½ molecules of water, if we accept the C_{20} formula, but in all probability this formula will have to be multiplied.

F. Baumstark,[1] by acting on an alcoholic solution of cholic acid with hydrochloric acid, has obtained an ether of the formula $C_{24}H_{39}(C_2H_5)O_5$, which splits up by caustic alkalies into cholic acid and ordinary alcohol, but when heated with alcoholic ammonia to 120° it is said to yield cholamide, $C_{24}H_{39}O_4H_2N$, which is identical with the amide obtained on heating ammonium cholate. The same chemist has also obtained ethyl-benzoyl-cholate, $C_{24}H_{38}(C_2H_5)(C_7H_5O)O_5$ by the action of ethyl-cholate upon benzoyl chloride.

H. Tappeiner[2] states that when cholic acid is oxidised by chromic acid (potassic chromate and sulphuric acid), it yields acetic acid and a fatty acid which is either palmitic or stearic, and a second acid which is crystallisable and melts at 250°. These facts remind forcibly of the relation of cholic acid to oleic acid, which splits up also into acetic and palmitic acids by the action of fused alkalies.

In an attempt to ascertain the nucleus of cholic acid by distillation with alkali, F. Baumstark obtained a semifluid oil, the nature of which, however, was not ascertained.[3]

[1] *Deut. Chem. Ges. Ber.*, vi. 1185, 1187.

[2] *Deut. Chem. Ges. Ber.*, vi. 1285.

[3] *Deut. Chem. Ges. Ber.*, vi. 1377, 1379.

When cholic acid is subjected to dry distillation it yields a volatile product said to exhibit the properties of phenol; and when distilled with alkalies, it yields volatile products between 150° and 280°, which give the Pettenkofer reaction.

Gorup Besanez states[1] that by melting the acid with potassic hydrate, acetic and propionic acids are formed, and a substance resembling dyslysin.

From these and other considerations, which will be insisted upon more particularly when treating of the Pettenkofer reaction, there is little doubt that between certain bile compounds and the fatty acids on the one hand, and certain benzene derivatives on the other hand, there exists some close relationship.

By acting on cholic acid with phosphorous chloride, a phosphorised product has been obtained according to some such reaction as is here given—

$$3C_{24}H_{40}O_5 + 2PCl_3 = C_{72}H_{114}P_2O_{15} + 6HCl.$$

This phosphorised product has been compared to certain compounds also containing phosphorus, which exist in brain and nerve matters. As we come to study the chemical constitution of the brain, it will be seen that this comparison is to some extent justifiable. But there is this difference presented by all the phosphorised principles present in brain matter, that they are also nitrogenous. Attempts to produce amidated compounds from the above-mentioned artificial phosphorised combination would no doubt yield singularly important and valuable results. Between the chemistry of the brain and bile compounds there is much in common.

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[1] *Ann. Ch. Pharm.* clvii. 282.

Choloidic Acid ($C_{48}H_{78}O_9$).—This acid, so-named by Demarcay, is derived, as already explained, from two molecules of cholic acid by the removal of one of water. It is a resinous white, friable substance, freely soluble in alcohol, but slightly so in ether, and altogether insoluble in water. The salts of the alkalies are soluble in water and alcohol, but do not crystallise. The barium salt is insoluble in water.

Redtenbacher has determined that when the acid is distilled with nitric acid it yields volatile fatty acids of the series $C_nH_{2n}O_2$, including acetic, butyric, caproic, œnanthylic, caprylic, pelargonic, and capric acids; oxalic and cholesteric acids remain behind, and a third crystallisable acid termed choloidanic ($C_{16}H_{24}O_7$).

In the transformation of choloidic acid into dyslysin under the influence of acids, each molecule loses three of water and becomes $C_{48}H_{72}O_6$, which is a body fusible at 140° C., and behaves like a resin.

Generalisation.—Among many of the substances described in the preceding sections there are several relations perceptible which are of great importance, both physiologically and chemically. Thus it has been shown that cholic, choloidic acid, and dyslysin each give, as an oxidation product, cholesteric acid. Choloidic acid yields also other products like to those given in a similar process by oleic acid. Moreover, all of these acids, and the conjugated glycocholic and taurocholic acids, as well as cholesterine, yield with sugar and sulphuric acid a reaction which Pettenkofer, at the time of his discovery, considered characteristic of bile compounds. Cholesterine ($C_{26}H_{44}O$) also yields cholesteric acid as an oxidation product. Now, in a subsequent chapter on the

Pettenkofer reaction, the relation of these biliary acids to oleic acid and the members of the fatty acid series generally will be still more fully developed; in the meantime, that there is a connection between the bile acids and cholesterine on the one hand, and the whole of these to oleic acid on the other hand, seems evident.

Again, the bile of the pig contains a resinoid acid termed hyocholic, of the formula $C_{27}H_{43}NO_5$, and this splits up in a manner similar to glycocholic acid, yielding glycocine and hyocholalic acid, thus:—

$$C_{27}H_{43}NO_5 + H_2O = C_2H_5NO_2 + C_{25}H_{40}O_4.$$

Hyocholalic acid may further split up into water and hyodyslysin, $C_{50}H_{76}O_6$, a body which is homologous with ordinary dyslysin. Further, the sulphuretted acid of pig's bile, which is complementary to hyocholic acid, has the formula $C_{27}H_{45}NSO_6$, and is related to taurocholic acid as hyocholic is to glycocholic acid.

Glycocine or Glycocoll ($C_2H_5NO_2$).—As stated while describing glycocholic acid, glycocine is produced by the decomposition of this substance into its proximate nuclei. It is also yielded as stated above by a similar decomposition of hippuric acid.

Most interesting is the derivation of glycocine from gelatin when boiled with dilute sulphuric acid, or with potash or soda—interesting, because, as will be shown hereafter, it is from albuminoïds similar to gelatin that the liver elaborates the bile, one of whose constituents is glycocholic acid which yields glycocine. By evaporation of its aqueous solution the base may be obtained in hard, sweetish crystals. The artificial synthesis of glycocine has been effected by several methods. Thus, Perkin and

Duppa[1] obtained it by acting upon an alcoholic solution of ammonia with bromacetic acid at an elevated temperature, the following reaction taking place:—

$$C_2H_3BrO_2 + 2NH_3 = C_2H_3O_2,NH_2 + NH_4Br.$$

That is to say, amido-acetic acid (glycocine) and ammonium bromide are produced.

A. Emmerling[2] performed the synthesis by passing a current of cyanogen through a saturated boiling solution of hydriodic acid, thus:

$$2(CN) + 5HI + 2H_2O = C_2H_5NO_2 + NH_4I + I_4.$$

Strecker found that by acting on uric acid with hydriodic acid, glycocine was also produced, and this fact led him to believe that uric acid contained a glycocine residue; Emmerling, however, says the fact is due to the presence of a cyanogen molecule in uric acid.

Glycocine is soluble in about 400 parts of cold water, but insoluble in alcohol or ether. It forms combinations with variable molecular proportions of hydrochloric, nitric, sulphuric, and oxalic acids; and many of these, such, for example, as the nitrate $C_2H_5NO_2,HNO_3$, crystallise. It also behaves as an acid towards bases, forming many soluble compounds with metallic oxides which are also crystalline. Compounds of zinc, copper, lead, barium, calcium, and silver are known.

It reduces mercurous nitrate and expels acetic acid from acetate of copper. Heated with strong potash solution, a transitory fiery-red colour is produced, ammonia is set free, and oxalic and hydrocyanic acids are formed in the solution. Beyond behaving as an acid and as a base, it behaves also, in some respects, like an alkaloid, forming combinations with salts which are crystalline.

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[1] *Q. J. Chem. Soc.*, xi. 31.

[2] *Deut. Chem. Ges. Ber.*, vi. 1351–1354.

A mixture of sulphuric acid and manganic dioxide gives, on distillation with glycocine, carbonic anhydride and hydrocyanic acid, thus—

$$C_2H_5NO_2 + O_2 = CO_2 + 2H_2O + HCN.$$

By the passage of nitrous acid through its aqueous solution, glycocine is resolved into nitrogen and glycolic acid, as follows—

$$C_2H_5NO_2 + HNO_2 = C_2H_4O_3 + H_2O + N_2.$$

The glycolic acid may be extracted by ether. According to E. Dreschsel,[1] an ammoniacal solution of glycocine, when treated with a solution of ammonium permanganate, yields carbonic, carbamic and oxamic acids; dioxide of manganese being precipitated. He also states that the same products are given by similarly treating leucine, tyrosin, or albumin, and he concludes that carbamic acid is always formed when carbon dioxide and ammonia act upon each other in the nascent state. From his experiments (which are not, however, of absolute precision) he infers that, in the formation of urea from albuminoids, glycocine, leucine, and tyrosin are first formed, and that these are subsequently oxidised into a carbamate, out of which some ferment arranges urea. This must be regarded, however, as highly problematical, notwithstanding that Schützenberger has recently obtained decisive evidence of the production of urea from albumin. Of this more anon.

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[1] *Journ. pr. Chem.* (2), xii. 417–426.

R. Engel states,[1] the colour-reaction said to be yielded by glycocine and alkalies is due, when observed, to impurities, and that the reactions with mercurous nitrate and copper sulphate are not sufficient to characterise it. He gives two new reactions, which are as follows.

With ferric chloride, glycocine gives an intense red colour, which disappears on the addition of acids, and is reproduced by ammonia. A drop of phenol and some sodium hypochlorite gives, with a solution of glycocine, a fine blue coloration; other amines, however, behave similarly.

Before concluding, it may be noticed that K. Kraut,[2] in a study of glycocine derivatives, states that when silver glycocine acts upon methyl iodide, the methiodide of methylic dimethylamidacetate is formed, from which oxyneurine can be produced. This fact is interesting by bringing into plausible relationship bodies which occur in the animal organism, and which must have a common origin—namely in albuminoïds.

Taurin ($C_2H_7NSO_3$).—This substance, which can be detected in the fæces, is obtained from taurocholic acid as described under that substance. Cloetta has detected it in small quantity in the lungs of the ox, and has established its identity with the substance named by Verdeil pneumic or pulmonic acid.

It is isomeric with sulphite of aldehyd-ammonium (C_2H_4O,NH_3,SO_2), from which, however, it differs in its properties. Taurin appears to be dehydrated isæthionate of ammonium, and was prepared synthetically by Strecker[1] as follows:—Isethionic acid (prepared from olefiant gas and sulphuric anhydride) in aqueous solution is neutralised with ammonia, and the solution on evaporation yields crystals of the salt $NH_4C_2H_5SO_4$, which, on heating to 230° C., loses water and yields taurin, thus—

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[1] *Bull. Soc. Chim.* (2), xxiii. 435–437; and *Compt. Rend.* lxxx. 1168.

[2] Liebig's *Annalen*, clxxxii. 172.

$$NH_4,C_2H_5SO_4 = H_2O + C_2H_7NSO_3.$$

R. Engel, however, points out[2] that the body thus obtained differs from taurin proper in its fusion point and by the fact that it yields ammonia when boiled with potassic hydrate. From further researches, he concludes that taurin is not isethionamide, but a glycocine or acid amide which may be synthetically prepared by acting on ammonia with chlorethylsulphurous acid. Engel shows its further similarity to glycocine by having prepared a basic salt of the formula $C_2H_6HgNSO_3 + HgO$.

Taurin crystallises in forms like quartz; it is soluble in 16 parts of cold water, but is insoluble in absolute alcohol (although it dissolves in weak alcohol) and in ether. On burning in the air, it yields sulphurous anhydride. Potash dissolves it, and on evaporation ammonia is evolved, while potassic sulphite and acetate are formed.

It is oxidised in the system, and the sulphur is excreted in the urine as sulphuric acid.

Cholesterine ($C_{26}H_{44}O$).—This beautiful substance, entering into the composition of bile, occurs still more largely in brain and nerve substance; it is also met with in the yelk of egg, the seminal fluid, and in blood attached to the corpuscles. It has been found in milk, the spleen, the excrements of various animals, in the *corpus luteum* of the cow, in peas, and other vegetable substances, &c. In several morbid products, as gall-stones, the fluid of hydatid ovarian cysts, and pus, cholesterine also occurs, while it is a common product of putrefactive changes in muscular tissue.

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[1] *Chem. Gaz.*, 1854, 388; and *Verh. d. phys.-med. Ges. zu Würzburg*, Bd. 2, S. 299.

[2] *Compt. Rend.*, lxxx. 1398–1400.

The quantity present in bile is variable, and is, according to Berzelius, one in 10,000, while, according to others, bile contains as much as 0·25 per cent.

From its ready solubility in, and crystallisability from alcohol or ether, it is easily obtained in a pure state; if required to obtain it free from fatty matters, this is best done by a process of saponification, by which the cholesterine is not attacked, and consequently may be readily extracted from the soap by ether.

Cholesterine is practically insoluble in water, and crystallises in beautiful pearly plates somewhat resembling naphthaline. These crystals may be obtained in a form containing 5 per cent. water of crystallisation which is expelled at 100° C. It fuses at 137° C., and at a higher temperature may be distilled unchanged, if care be taken; but at still higher temperatures it decomposes.

By heating cholesterine during some hours in sealed tubes with various acids, certain compounds termed cholesterides are obtained (Berthelot), resembling saccharides in their general nature. These may be regarded as the ethers of cholesterine (itself a monobasic alcohol, $C_{26}H_{43}HO$, according to Gerhardt). Thus the following compounds have been obtained — butyrocholesterine, $C_{26}H_{43},C_4H_7O_2$; stearocholesterine, $C_{26}H_{43},C_{18}H_{35}O_2$: and benzocholesterine, $C_{26}H_{43},C_7H_5O_2$. They are white fusible bodies, and but sparingly soluble in hot alcohol, but dissolving easily in ether. By the action of alcoholic solution of potash, they decompose, yielding cholesterine and the various acids from which they are relatively constructed. Sodium cholesterate, $C_{26}H_{43}NaO$, is produced by the action of metallic sodium upon cholesterine dissolved in petroleum spirit. This body, when heated with ethyl iodide, gives cholesteryl oxide.

Cholesteric acetate, $C_{26}H_{43}(C_2H_3O)O$, is prepared by the action of acetyl chloride on sodium cholesterate or cholesterine.

Cholesteryl chloride, $C_{26}H_{43}Cl$, may be obtained by acting upon cholesterine with phosphorous pentachloride; when decomposed with aqueous potash it yields cholesterine and potassic chloride.

Cholesterylamine, $C_{26}H_{43}NH_2$, results when the body $C_{26}H_{43}Cl$ is digested with alcoholic ammonia; it is crystalline, and melts at 104° (Henry).

The action of terchloride of phosphorus upon cholesterine yields neutral phosphorised bodies difficult of purification, and resembling, according to Gorup Besanez,[1] the so-called myelin; this, however, is only partially true, as myelin is also nitrogenous in character. Strong sulphuric acid removes water from cholesterine, and gives rise to the production of three hydrocarbons of the formula $C_{26}H_{42}$ named cholesterilin.

Nitric acid oxidises cholesterine, and yields (like the biliary acids) cholesteric acid, $C_8H_{10}O_5$, which is a yellow, deliquescent substance readily soluble in alcohol; other acids of the series $C_nH_{2n}O_2$, and oxalic acid, accompany the cholesteric acid.

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[1] *Ann. Ch. Pharm.* clvii. 284.

By oxidation of a milder character, such as is presented by a mixture of sulphuric acid and potassic dichromate, a white amorphous acid, termed oxycholic, $C_{23}H_{40}O_6$, is produced, and certain members of the fatty acid series.

Latschinoff has studied[1] the oxidising action of potassium permanganate upon cholesterine, and has obtained three different acids whose salts he has separated by the use of different solvents; the acids are—cholesteric acid, $C_{26}H_{42}O_4$; oxycholesteric acid, $C_{26}H_{42}O_5$; and dioxycholesteric acid, $C_{26}H_{42}O_6$.

By the action of bromine upon cholesterine dissolved in carbon disulphide, an additive product of the composition $C_{26}H_{44}OBr_2$ is obtained. It crystallises in white needles, and is insoluble in water, but dissolves readily in ether. Sodium amalgam reconverts it into cholesterine.

Cholesterine rotates a ray of polarised light to the left. When evaporated with a drop of nitric acid at a gentle heat it leaves a yellow spot, which turns red when moistened with ammonia. By heating with a mixture of 2 or 3 volumes of strong hydrochloric or sulphuric acid and 1 volume of moderately dilute ferric chloride solution, and evaporation to dryness, a reddish violet residue is obtained.

In strong sulphuric acid, cholesterine dissolves to a reddish colour, and on the addition of sugar (concentrated solution) the Pettenkofer reaction is exhibited.

E. Schulze has shown[2] that sweat contains, besides cholesterine, a modification of the same principle termed by him isocholesterine. It is particularly distinguished by depositing from its alcoholic solution as a translucent jelly; this was when it had been obtained from its benzoate by the action of potash. The author of this treatise has often observed, however, cholesterine from normal sources to behave similarly when recrystallised from benzene, and hence it appears doubtful whether more than one cholesterine really exists; a surmise which is supported by the identity of reactions and properties presented by cholesterine and so-called isocholesterine.

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[1] *Bull. Soc. Chim.*, xxvii. 456.

[2] *Journ. Chem. Soc.*, vol. xi. (ser. 2), p. 513; and *J. pr. Chem.* (2), vii. 163–178.

BILE PIGMENTS.

Bilirubin ($C_9H_9NO_2$).—Of the biliary pigments, that which has been best studied is bilirubin, also called cholophœine. It is readily prepared by extracting inspissated bile, or, what is better, crushed gall-stones,[1] successively with water, alcohol, dilute hydrochloric acid, boiling alcohol, and ether; the residue is dried and then extracted with boiling chloroform, which assumes a yellow colour as the bilirubin dissolves. The chloroform extracts when saturated, deposit minute crystals of bilirubin on cooling, but it is best to concentrate the solution by distillation, and to precipitate the final extract with alcohol.

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[1] Maly (*Annalen der Chemie*, clxxv. 76, 77) has given the following analysis of ox gall-stones:—

Soluble portion	=	18·09
Ethereal extract (fat)	=	5·28
Phosphates and bases	=	1·41
Bilirubin	=	28·10
Residue and loss	=	47·12

The reasons for using the above method are as follows:—The water extracts whatever is soluble therein, such as mucus, salts, &c.; the alcohol takes out cholesterine, fatty and biliary acids; the acid decomposes the lime salt of bilirubin (for it exists in combination in gall-stones), and removes the lime; the alcohol and ether finally complete the extraction of soluble matters produced by the previous use of the acid, and dissolves only traces of bilirubin, which is, however, easily soluble in chloroform. It is also soluble in bisulphide of carbon, turpentine, and benzene.

In the form of powder, bilirubin is of a brilliant red colour; its crystals have a bluish shade over the red. The biliary calculi of oxen derive their yellow colour from the presence of bilirubin, and are much valued by artists for compounding pigments of a brilliant tint and durable character.

Städeler assigned to bilirubin the formula $C_{16}H_{18}N_2O_3$, but he afterwards withdrew this formula, and taking more extensive results obtained by Thudichum,[1] constructed upon them the theory of bilirubin as a hexabasic acid. Thudichum, however, has protested[2] against this, and indeed his work is entirely opposed to the conclusions drawn by Städeler.

Maly[3] has also occupied himself with studies upon bilirubin; but as his results, so far as they have been established, are merely confirmative of those obtained previously by Thudichum, we shall confine ourselves to the researches of the latter. He has shown that from a solution of bilirubin in very dilute ammonia, nitrate of silver precipitates the compound $C_9H_8AgNO_2,H_2O$. Chlorides of barium and calcium, precipitate from a similar solution, compounds of a red colour and of the composition $2(C_9H_8NO_2)Ba,C_9H_9NO_2+2H_2O$ and $2(C_9H_8NO_2)Ca,C_9H_9NO_2,2H_2O$. Beyond these, the same chemist has also described the following preparations :—

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[1] 10th Report Med. Officer of Privy Council, 1867, pp. 240-251; also *Journ. f. pract. Chemie*, 104 (1868) 4.

[2] *Journ. Chem. Soc.*, May 1875.

[3] Maly's researches are summarised and criticised by Thudichum in an open letter to the Vienna Academy. See *Chemical News* of April 13 and 21, 1876.

Basic silver salt	$C_9H_7Ag_2NO_2$
Neutral barium salt	$2(C_9H_8NO_2)Ba,2H_2O$
,, calcium salt	$2(C_9H_8NO_2)Ca,2H_2O$
Acid zinc salt	$2(C_9H_8NO_2)Zn,C_9H_9NO_2,2H_2O$
Basic lead salt	$C_9H_7PbNO_2$

If bilirubin be dissolved in caustic or carbonated alkali, and the solution exposed to the air for some days, the product turns green, and on addition of hydrochloric acid, green flakes of biliverdin ($C_8H_9NO_2$) are produced, and may be purified by regeneration from an alcoholic solution.

By the action of nitric acid containing nitrous acid, upon bilirubin, a play of colours is produced, passing from green, blue, violet, and red to yellow.

Brücke modified this test, and recommends the use of boiled pure nitric acid and the cautious addition of sulphuric acid to the bottom of the test-tube. E. Fleischl[1] has simplified the test by using a concentrated solution of sodium nitrate instead of the freshly boiled nitric acid.

If concentrated nitric acid be added to an ammoniacal solution of bilirubin, a blue precipitate is formed at a certain stage. This is soluble in alcohol, and has been termed cholocyanin; it presents a characteristic spectrum. Concentrated sulphuric acid gives with bilirubin a green solution, and this in contact with a moist atmosphere, or on the addition of water, gives, among other products, cholothalline, $C_9H_{11}NO_3$.

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[1] *Chem. Centr.* 1875, p. 568.

There is no established connection whatever between bilirubin or other biliary pigments and the colouring-matter of blood; it is necessary to state this emphatically on account of the existence of erroneous statements and impressions to the contrary. Thus, Maly[1] obtained by heating bilirubin suspended in water with sodium amalgam in excess, a body which he termed hydrobilirubin, and which he viewed as identical with the colouring-matter of urine; but Thudichum[2] has demonstrated the inaccuracy of the latter proposition.

When dry bilirubin is exposed to the dry vapour of bromine, it forms the substitution product $C_9H_7Br_2NO_2$: this is stable at 100° C., and constitutes a dark blue-black powder soluble in dilute acids to a blue colour. Thudichum has also described the following compounds: C_9H_8BrNO, and $C_9H_8BrNO,C_9H_9NO_2$. This chemist had by earlier experiment fixed the atomic weight of bilirubin at 163, a figure which is confirmed by the direct bromination experiment leading to the production of $C_9H_7Br_2NO_2$: the only doubt about this formula which now remains, attaches to the hydrogen; this figure may possibly have to be increased.[3] Iodine vapour has no action upon bilirubin, but chlorine gas seems to give several substitution products, among them $C_9H_5Cl_4NO_2$.

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[1] *Ann. Chem. Pharm.* 1872, No. 7, p. 77.

[2] *Journ. Chem. Soc.*, May 1875.

[3] See analyses executed by the author for Thudichum, and described on p. 9- of Thudichum's open letter.

Bilirubin is the substance which is supposed to give the colour to the skin in 'yellow jaundice,' while 'black jaundice' colour is due to the retention of biliverdin; these principles may be extracted from the skin in jaundice (bilirubin by chloroform, and biliverdin by alcohol[1]).

As before stated, the further history of the biliary pigments after they mingle with the contents of the intestinal canal is practically unknown.

Biliverdin ($C_8H_9NO_2$).—As already explained under bilirubin, this substance is best produced by Heintz's process, which consists in passing a current of air through an alkaline solution of bilirubin and precipitation of the resulting solution by means of hydrochloric acid.

Biliverdin is soluble in alcohol, benzene, and carbon disulphide, but insoluble in water, ether, and chloroform.

In a further investigation of the properties of biliverdin, Thudichum[2] has confirmed his hypothesis according to which it is produced from bilirubin by the reaction $C_9H_9NO_2 + O_2 = CO_2 + C_8H_9NO_2$. Städeler's hypothesis, that in the change to biliverdin, bilirubin takes up one molecule of water and one of oxygen ($C_{16}H_{18}N_2O_3$ $H_2O + O = C_{16}H_{20}N_2O_5$) is no longer tenable. By the action of dry bromine vapour upon dry biliverdin, and subsequent heating of the product to 100° in a current of dry air, Thudichum has obtained a monobrominated product, $C_8H_8BrNO_2$. This compound is perfectly black, insoluble in ether, and only slightly soluble in alcohol. When biliverdin is dissolved in caustic soda and exposed to the action of sodium amalgam, a change is brought about which has not yet been precisely ascertained.

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[1] See *Chem. News*, May 12, 1876.

[2] *Journ. Chem. Soc.*, July 1876.

The product, however, which is termed hydro-biliverdin, is distinct from a compound produced similarly from bilirubin.

An ammoniacal solution of biliverdin is not precipitated by calcium or barium chloride; but the acetates of lead, silver, and mercury yield precipitates in an alcoholic solution of the colouring matter.

Bilifuscin ($C_9H_{11}NO_3$) (?).—To obtain this pigment, gall-stones may be powdered and extracted, first with ether, then with very dilute acid, as preliminaries to extraction by absolute alcohol. The bilifuscin dissolves in the boiling alcohol to a brown colour. It is insoluble in water, ether, and chloroform, but is soluble in alkalies, and reprecipitated by hydrochloric acid in brown flakes.

It furnishes calcium and barium combinations by precipitation of its ammoniacal solution with the respective chlorides of these metals.

Its precise formula is yet doubtful; Städeler regards it as bilirubin plus one molecule of water; but as his formula for bilirubin is wrong, dependence cannot be placed upon that for bilifuscin.

Other Biliary Pigments.—Biliprasin is said to be obtained by extracting inspissated bile or gall-stones successively with ether, hot water, chloroform, dilute acid, and boiling chloroform; the residue on extraction with alcohol takes up biliprasin to a green colour.

Bilihumin is left in the residue after the extraction of the foregoing pigment.

According to Thudichum a number of other colouring matters which may be spectroscopically identified are to be found in certain diseased processes terminating in the production of calculi.

Other Constituents of Bile.—The only remaining constituents of bile are lecithin and choline; the one is a phosphorised and amidated fat, the other is the ammonium-base it yields on decomposition. As we shall have to enter more fully into the study of these principles in treating of brain chemistry, their consideration is reserved till then.

CHAPTER VIII.

THE LIVER; ITS FUNCTIONS. GLYCOSURIA AND DIABETES.

In Chapters VI. and VII. we have studied the nature and chemistry of that liquid the secretion of which constitutes the principal function of the liver, and in our present study it will be important to bear in mind what is taught in Chapter IX. regarding the presence of sugar in the blood.

The liver is the largest glandular organ in the body, being from 50 to 60 ounces in weight, and consisting of cells which seem to be the seat of its specific functions. It is supplied with blood vessels and bile ducts, interspersed with lymphatics and nerves. Fat and bilirubin may be contained in it, and it also furnishes albumin, mucin, glycogen, sugar and biliary acids. When recently extracted from the body, the liver presents an alkaline reaction, but becomes acid on standing. Boiling water extracts from the liver, lactic and volatile fatty acids, inosite, xanthine, hypoxanthine, uric acid, and leucine. Its ash furnishes potassium and phosphoric acid.

There are various diseases of the liver, the best known being so called degeneration, or 'bacony liver,' but of the chemical causes underlying it, or of the chemical interpretation to be placed upon it, we are without knowledge.

There can be no doubt that the principal function performed by the liver consists in the elaboration of bile and its secretion. This elaboration is effected from the constituents of the blood which is presented to the liver, but we are totally ignorant of the profound changes which must constitute this important process. The whole process is controlled and regulated no doubt by the nervous system, a fact which A. Socoloff has brought to bear in explanation of some otherwise uninteresting experiments detailed[1] by him. The author found that the secretion of bile is distinctly increased by the introduction of glycocholate of sodium into the stomach or blood, but from a further consideration of these and other results, he concludes that the phenomenon is one of peculiarly nervous origin, and due in the particular instance cited to the irritating properties of the biliary acids.

Socoloff's paper is characteristic of many others of a like kind, and equally worthless; so worthless indeed that we shall disregard them, and for this reason. Between the methods of experiment having themselves no safe warranty of employment, and the results, there is no direct connection; it is impossible to reason from effects to causes, or *vice versâ*, and as the methods of experiment are generally ill-considered, and the results misunderstood or misinterpreted, it is best to leave them out of consideration. As regards, therefore, the production of bile from the elements of the blood we know at present no more than the fact.

It has been thought that the liver is one source of the colourless corpuscles of blood, but here again we are without absolute knowledge. We therefore pass on to consider a further function known to be resident in the liver.

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[1] Pflüger's *Archiv. für Physiologie,* xi. 166–177.

Bernard and Hensen discovered in the liver a kind of dextrin of the formula $C_6H_{10}O_5$, and they concluded that it was produced through a decomposition of albumin exerted by that organ. Subsequently, it has been ascertained by Dr. M. Foster, Bernard, Pavy, and others, that a similar amyloid matter is found in other forms of life (Entozoa, larvæ of flies, solidified lung of pneumonia, &c.) accumulated in structures having one feature in common with the liver, namely a limited supply of oxygen. Pavy has used this fact as an argument in theories which we must hereafter consider, but for the present it cannot be regarded as decided whether this character in common is anything more than the utmost accident. More especially must this precaution be observed since glycogen has been stated also to occur in the transversely striated muscles. Abeles found[1] this substance also in the spleen, lungs, and kidneys of dogs fed exclusively for some days previous on bread.

The characters of glycogen are very simple; when dry it is a yellowish-white powder, but it may take up one or two molecules of water, and become gummy. Its aqueous solution polarises light to the right four times as intensely as dextrose sugar. In alcohol it is insoluble. With iodine it gives a violet or maroon-red coloration. Its aqueous solution dissolves oxide of copper, but exercises no kind of reducing action on the potassio-tartrate of copper. When boiled with dilute acids, or when subjected to the action of saliva, pancreatic juice, serum of blood, or cold prepared extract of liver, it is transformed into glucose by the assimilation of a molecule of water. It is readily prepared by mincing a fresh liver and boiling with water, filtering, and pressing. The filtrate is then concentrated and precipitated with much strong alcohol, when yellowish-white flocks are thrown down, consisting of impure glycogen. It may be purified by boiling with caustic potash, dilution with water, and reprecipitation by absolute alcohol. Or the glycogen may be precipitated from the concentrated aqueous extract of liver by means of glacial acetic acid.

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[1] *Chem. Centr.* 1876, 230.

As regards the precise method by which the liver elaborates it from the blood, little definite knowledge is possessed. But from what has been ascertained it may be formed from albumin alone, although with fowls a mixed diet of starchy and albuminous matters is most favourable to its production.

Numbers of researches bearing upon this question have been published, but in most of them it is impossible to draw any definite conclusions from the experiments described. S. Wolffberg has discussed[1] the whole question, and after reviewing the views and experiments of Bernard, Voit, Pettenkofer, Vallentin, Bauer, Dock, and others, concludes from his own investigations that glycogen is an intermediate decomposition product of albumin in the animal organism. In connection with this view it may be interesting to bear in mind two facts, viz., that the liver undoubtedly produces bile by the decomposition of albumin, and that certain albuminoïds,

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[1] *Zeitschr. f. Biologie*, xii. 266–314.

(such as chondrin) yield glucose when decomposed by hydrating agents (see Chapter on Albuminoïds). J. Forster[1] finds that when sugar is injected into the veins of dogs which have been kept without food for several days, the amount of glycogen in the liver is increased. It cannot be supposed that glycogen is formed in the economy from sugar, and J. Forster concludes that the increase of glycogen arises from an increased decomposition of albuminöids brought about through the sugar. Thus it arises that one of the points at issue between those experimentalists who have devoted time to this matter is this: is glycogen formed directly from bodies introduced with the object of increasing its amount (as maintained by Pavy and others), or do these substances only contribute indirectly by being themselves oxidised, and thus protecting the glycogen from change, as maintained by Tieffenbach and Weiss and others? V. Mering[2] attempts to decide this question, and he has found that the assimilation of a number of substances such as grape-sugar, cane-sugar, milk-sugar, fruit-sugar, inulin, lichenin, glycerine, arbutin, gelatin, and albuminates, produces a considerable accumulation of glycogen in the liver. On the other hand he found that inosite, mannite, quercite, erythrite, and fats failed to behave in the same way. To sum up this part of our subject, it may be said that of the history of the production of glycogen we do not know sufficient to decide precisely regarding it.

Opinion is by no means unanimous either as to the final destiny of liver glycogen; some physiologists maintain that it passes from the liver in an unaltered state, and is finally oxidised in the circulation, while others hold that it is changed while yet in the liver into sugar, and this passing by the hepatic vein into the system becomes oxidised. This latter view is supported strongly by Bernard, and to a large extent has been adopted by physiologists who write of the 'glycogenetic function of the liver.' This theory certainly derives weight from the fact that dead liver is capable of quickly converting glycogen into sugar. Pavy, however, who ardently supported it at first, became the first to as strenuously oppose it on the alleged ground that no sugar is made in the liver in health.

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[1] *N. Rep. Pharm.* xxv. 773–739.

[2] Pflüger's *Archiv. f. Physiologie*, xiv. 274–284.

Nevertheless some sugar can be found in hepatic blood, and it has been shown by Thudichum[1] that Pavy's experiments are by no means conclusive.

According to Tiegel, the blood corpuscles undergo disintegration in the liver, yielding a ferment which transforms starch into sugar, but v. Wittich has shown[2] that even serum yields such a ferment by extracting its alcoholic precipitate with glycerine. He has also obtained a diastatic ferment from the parenchyma of the liver when it has been quite freed from blood. It appears to be formed in the cells, and is partly poured out with the bile.

W. Epstein and J. Müller[3] seem to have confirmed in some measure the experiments of v. Wittich.

Liebig showed that the liver itself, when finely minced and suspended in water, ferments and evolves carbonic dioxide and hydrogen, and Béchamp has repeated and extended these observations, and has shown that the same occurs even when the liver has been washed in water containing phenol. Béchamp also showed that the fermentation is independent of the presence of micrococci and bacteria, and W. K. Yasnopolsky[1] has confirmed these views. So that altogether it seems to be fairly established that the liver contains certain active ferments; it also produces glycogen, which admits of being changed into sugar by means of the said ferments. We must now apply this knowledge in attempting to explain an artificial form of diabetes termed glycosuria, and the true disease itself.

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[1] Thudichum's *Chemical Physiology*, p. 8.

[2] Pflüger's *Archiv.* vii. 28–32.

[3] *Deut. Chem. Ges. Ber.* viii. 679–682.

On the theory that sugar is formed in the liver and oxidised in the blood, a lack of oxidising power was conjectured to constitute the disease known as diabetes mellitus, since in this disease, sugar is voided in the unchanged state.

Rollo alleged[2] that 'this disease consists in an increased morbid action of the stomach with too great a secretion, and an alteration in the quality of the gastric fluid, producing saccharine matter by a decomposition of the vegetable substances taken in with the food, which remains unchanged.' Others, however, and among them Dr. Baillie, maintained that the morbid action resided in the kidneys; but Rollo argued that from their very nature these organs are incapable of forming sugar, simply acting as separating agents; he yet allowed that they might become morbid through an increased activity and sympathy to which they may be subject in such a disease, and he thus explained a fact he himself observed, viz., that in certain cases the urine contains more sugar than the blood. In consonance with these views, sugar-forming foods were avoided in the treatment of the disease, while such oxidising agents as potassic chlorate and nitric acid were recommended for administration.

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[1] Pfluger's *Archiv.* xii. 78–86.

[2] Rollo on *Diabetes Mellitus*, p. 387.

We pause here, to remark how characteristic such reasoning as this is, even in these days, of some medical men who fail to perceive the common requirements of logical science. Assuming that by means of oxidising agents all the sugar existing in the blood admits of oxidation, it by no means follows that because the sugar is thus destroyed, the causes of its formation are also removed, for its formation is the revealing characteristic of the disease! Moreover, it is very doubtful whether the sugar which may be present in the blood can be oxidised in this way. Dr. Day, of Geelong, has recommended peroxide of hydrogen for this purpose, although he admits that it does not remove the causes of the disease. We know nothing of what relief it may afford to sufferers, but it certainly does not appear to act by virtue of its oxidising powers over sugar. This the writer has ascertained for himself, at least so far as regards the diabetic sugar present in urine, and what holds good with urine most probably is true of the blood.[1] But to return from this digression.

With the view of testing the prevailing theory of diabetes, Dr. A. Dupré made some experiments which were published at the time in the *Practitioner*. He administered known amounts of fruit-sugar (in the form of honey) to a diabetic patient, and estimated the sugar voided in the urine. In this way it was shown that all the fruit-sugar contained in the administered honey was oxidised in the system; it therefore becomes clear that diabetes is not to be explained as due to a lack of oxidising power in the blood. Dupré went further than this in his conclusions; he thought his results pointed to the conclusion 'that the sugar found in the urine has not previously existed ready formed in the blood, but has been formed only in its passage through the kidneys.'

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[1] *Chemistry of Diabetes Mellitus*, by C. T. Kingzett. *Chem. News*, vol. xxxii. p. 184.

The correctness of the first conclusion is supported by Bernard's observation, that an artificial diabetes (glycosuria of Pavy) can be developed in dogs and rabbits by irritation of the fourth ventricle of the brain with a needle, whereby sugar is developed in the blood, and passed in the urine.

The other conclusion is by no means so clear; Lehmann and Dupré both found that the percentage of sugar in the blood in cases of diabetes generally amounts to 0·04 per cent. only, a quantity not comparable to that excreted in the urine, but nevertheless such a conclusion is in opposition to all our knowledge of the functions of the kidneys. Moreover, other observers differ from Lehmann and Dupré in their determinations of the sugar present in diabetic blood; thus Thudichum found in one case as much as 2 per cent. sugar. Dr. Dalton also determined the amount of sugar present in a normal liver immediately after removal from the body at 0·25 per cent.

That diabetes is an exceedingly ill-understood disorder is evident from other points of view. For instance, Dupré observed that the administration of sugar in his experiments caused a decrease in the amount of urea secreted, a fact previously noted by F. Hoppe.[1] In this disease, also, lactic acid has been alleged to make its appearance in the saliva, and aceton in the stomach and urine; as regards aceton, however, this is more than doubtful, because the tests employed in its detection are tests also for alcohol.

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[1] *Arch. f. Path. Anat.* x. pp. 144–169.

Glycosuria may be variously produced. Thus Wickham Legg found that if the *ductus choledochus* of a cat were tied, while no sugar was found in the urine within five or six days after puncture, yet without tying the duct, glycosuria commenced within an hour after puncture. Afterwards v. Wittich found that the tying of the duct diminished the amount of glycogen in the liver, and caused glycosuria. In an endeavour to account for this fact observed by v. Wittich, experiments were made by E. Kulz and E. Frerichs,[1] and their results were claimed by them to show in common with previous experiments by Legg, that it was due to the liver not producing more glycogen beyond what existed at the time of tying.

Bernard's observation of the causation of glycosuria by a nervous interference paved the way for other discoveries of a similar nature. Thus Pavy found that a division of certain parts of the sympathetic system occasioned the presence of sugar in the urine. In his more recent researches[2] Pavy condemns, on the basis of experiment, Schiff's hypothesis, in which the escape of sugar from the liver, and incidentally, the production of glycosuria, are supposed to be brought about by the development of a ferment in the blood flowing to the liver as a result of the hyperæmia which succeeds those operations on the nervous system which give rise to artificial diabetes. In some experiments upon dogs, Pavy has found that when defibrinated arterial blood is injected into the mesenteric vein, sugar is developed in the circulation; in the urine the sugar amounted to from 10 to 15 grains per fluid ounce. Inasmuch as venous blood fails to produce these results, Pavy concludes that the production of glycosuria through influences on the nervous system is due to a vaso-motor paralysis affecting the vessels of the chylo-poietic viscera, by which process the blood reaches the portal system without having been de-arterialised. Pavy finds the support of his theory in the results of experiments in which animals were made to breathe oxygen; in several experiments upon dogs saccharine urine was thus developed, but other experiments, however, failed in this respect; so also with frogs the results were partly negative although chiefly affirmative. Tieffenbach had previously determined that artificial respiration with air is sufficient to produce glycosuria, and Pavy confirms this observation, as also one made previously by Dr. Richardson and by Schmiedeberg to the effect that inhalation of carbonic oxide produces a like result. A similar action of puff-ball smoke is explained by Pavy as due to its contained carbonic oxide; it should be remarked, however, that the physiological effects of pure carbonic oxide are totally distinct from those of puff-ball smoke.

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[1] Pflüger's *Archiv. f. Physiologie*, xiii. 460–468.

[2] *Proc. Roy. Soc.* vol. xxiii. p. 539, and vol. xxiv. p. 51.

In explaining the power of oxidised blood to convert the glycogen of the liver into sugar, Pavy looks upon this event as only a part of the whole truth, nor does he regard the action as due directly to the oxygen in the blood, but rather to the action of the de-arterialised blood as a ferment. Pavy's theory is in no wise deserving of full credence. In the first place he is credited with having shown that temporary glycosuria can be induced by impeding respiration, and unless it can be shown that in such case, blood reaches the liver in an arterial condition (an incomprehensible result), the fact, if true, is directly opposed to his more recent experiments above described, and irreconcilable with the conclusions he has drawn from them. Again, if oxygen in the blood gives rise to a ferment, then carbonic oxide, acting (as Pavy says it does) like oxygen, must give rise to a ferment also; but on chemical grounds it is at once seen that the ferments (if such exist at all) cannot be identical; hence the production of glycosuria by the two agents must be brought about in different ways in the two instances, and then again such cases of artificial diabetes must be explained differently to the ordinary disease of that name.

Pavy's conclusions admit of experimental criticism as follows: If glycosuria be due to the transformation of amyloid substance into sugar through the agency of a ferment present in oxidised blood, then if this dextrin-like body be isolated (as it can be) and treated with arterial blood out of the body, it should give rise to the formation of sugar. The same result should be attained by blood saturated with carbonic oxide. But even if affirmative results were attained, they would be of little value if the statement be true, as alleged, that blood serum contains a ferment possessing this power. If blood serum contains such a ferment, or if the liver contains one (and both are said to), then the amyloid substance, both in health and during diabetes, should be transformed into sugar; in truth, such appears to be the case, the difference being that in health the sugar is oxidised in the blood, whereas in diabetes and glycosuria it is voided in an unchanged state.

Thus, in spite of all the researches which have been made on these vexed questions, we are left without 'a plausible theory or a rational treatment of diabetes' (Thudichum). Organic diseases affecting the brain and spinal cord, external injuries to the brain, and certain influences on the sympathetic nervous system, are known often to precede diabetes, and perhaps to lead to it, and these observations, supplemented by Bernard's famous, and Pavy's skilful experiments, would seem to indicate that diabetes, as we recognise it in its chief characteristic (the presence of abnormal quantities of sugar in the blood and urine), represents a factor of interference of the proper functions of the blood, as governed solely by the nervous system. It becomes therefore of great and necessitated importance, that research should be directed to the chemical and anatomical investigation of the brain and other nervous centres in cases of death from diabetes mellitus. The disease seems to exist in many forms which may or may not be related to the same original causes, but in the foregoing remarks the subject has been treated as a whole for the sake of convenience, and in order to carry out the more immediate object of this work, viz., the application of chemical science to physiology and pathology.

PART III.

NUTRITION; OR 'WORK AND WASTE'

CHAPTER IX.

CHYLE, LYMPH, AND BLOOD.

CHYLE.

Chyle is the digested fluid absorbed by the lymphatics—or lacteals, as they are called—of the intestines. These lacteals form networks in the walls of the small intestine, and send blind prolongations into the little processes termed villi. The lymphatics have trunks which lead through the mesenteric glands and discharge themselves into the receptacle of the chyle, a dilated part of the lower end of the thoracic duct. The chyle is ultimately poured into the general circulation near the junction of the left internal jugular and subclavian veins.

A large part of the chyle, while yet in the intestine, is absorbed directly into the blood-system. It constitutes the fluid which yields to the blood all those matters which are necessary to maintain all parts of the body in a proper state of nutrition, and to atone for those processes of work and waste which we shall see hereafter constitute the essential conditions of life.

It is an opalescent creamy-looking fluid, deriving its yellowish white or slightly red colour from the suspension of fatty matters in the form of an emulsion. It also contains fibrin, or a form of principle immediately antecedent to fibrin; hence, after removal from the body, it speedily coagulates in the same way as blood. Chyle is of an alkaline reaction and a saline taste, and contains potassium-albumin, casein, and seralbumin, also lactates, sugar, urea, and alkaline salts, besides white and red corpuscles. It has been conjectured that these corpuscles form in certain lymphatic glands through which the chyle passes, as already explained.

It appears that the amount of fibrin increases as the chyle reaches that point where it is discharged into the blood; hence it is supposed that in its passage, it is gradually formed from the albumin present.

The following analyses[1] express the general composition of chyle in full digestion and while fasting:—

	In Full Digestion.	Fasting.
Water	91·8	96·8
Solids	8·2	3·2
Fibrin	·2	·09
Albumin	3·5	2·30
Fats	3·3	·04
Extractives	·4	·77
Salts	·8	

Hensen has published[2] the following analyses of supposed chyle obtained on different days from a lymphatic fistula:—

Water	91·0	96·3	
Albumin	1·7	3·9	mean 3·15
Fat	0·28	3·69	
Alcoholic extractives	0·021	0·183	
Water extractives	0·104	1·04	
Cholesterine	0·018	0·102	
Ash	0·643	1·09	mean 0·768
Iron (mean)	0·0022		

It cannot be said that human chyle has been properly examined, but few opportunities presenting themselves for effecting its complete study. Chyle may be regarded as dilute and imperfectly formed blood; thus, while the blood of a horse contains 22 per cent. solid matter, its chyle furnishes only from 4 to 9 per cent. solid matter.

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[1] Ralfe's *Physiological Chemistry* (authors not given).

[2] Pflüger's *Archiv. f. Physiologie*, x. 94–113.

No fibrin is found in the chyle as it is absorbed by the lacteals of the intestines, an observation which lends probability to the view already expressed, that it is formed in its passage to the thoracic duct from the soluble albuminous principles present. Among the extractives not only urea, but leucine and tyrosin are stated to have been found. The ash resembles that of blood, and yields chiefly potassium salts; phosphate, carbonate, and chloride of sodium being also present as well as a little calcium and magnesium.

Before entering the blood, chyle is always mixed with a considerable amount of lymph, and Bidder has calculated from some experiments on animals, that in an adult man there are discharged from the thoracic duct into the subclavian vein about 6·6 lbs. of true chyle mixed with 22 lbs. of true lymph in twenty-four hours. The emulsive state in which the fat exists in the chyle has been alluded to under the processes of digestion. In certain diseased processes—for instance, chylous urine—a persistence of fatty emulsion is observed in arterial blood, and occurs also in the disease cited, in the urine.

LYMPH.

Lymph may be regarded as transuded serum of blood which has been reabsorbed from the tissues, and carried back to the circulation by the lymphatics. Like the blood, it is alkaline, and consists of a plasma and corpuscles which, however, are all white; it contains about 5 per cent. solid constituents, and is, indeed, diluted blood-serum, from which the tissues have already taken what they require for their proper nourishment. The serum of blood contains about 8 per cent. solid matters. It is calculated that a quantity of fluid equal to that of the blood is poured daily from the lymphatic system into the former.

Lymph constitutes a clear, nearly colourless, or straw-coloured fluid, and of composition very like to that of chyle, except that it contains less fibrin and fatty matter. Its fat occurs in the form of globules, and its ash presents a further difference from that of chyle by having a predominance of sodium salts; it also contains lactic acid.

For the purposes of ordinary study, it may be obtained from a blister, but its whole constitution is not well known by reason of the difficulty experienced in obtaining sufficient quantity in a healthy state.

In scrofula and tuberculosis, both lymph and chyle are often deranged simultaneously with the diseased glands, and Thudichum states it is probable that improper nutrition has the main share in causing these diseases in many children.

BLOOD.

Of the nutrient fluids contained in the body, blood is from every point of view the most important. Elaborated from the food by virtue of the digestive and other processes already described, it serves to supply to the body fresh material in place of that which is worked up —worn out—by the processes of life. It also dissolves and carries away those products which result from the processes just alluded to, and it is through the blood that the great process of oxidation by respiration is effected. Blood consists in 1000 parts of about 795 water and 205 solids, these latter being made up, as might be conjectured from the known composition of chyme and chyle, of albumin, fibrin, colouring matter containing iron, fatty matters, extractives, and salts. But inasmuch as it constitutes the drainage-system of the body also, or the stream which absorbs the effete products of life-changes, these latter are also contained in it and complicate its constitution. Owing, however, to our imperfect knowledge of the real steps involved in the wear and tear of the animal tissues, it is difficult to say in regard to some of the blood constituents which are principals and which are excrementitious.

Blood is of an alkaline reaction and saline taste, with a specific gravity ranging between 1050 and 1060. As it exists in the body, it has a temperature of 36·5° to 37·8° C., a fact which will require more particular study hereafter, in considering the meaning of vital force; it is sufficient here to remember that animal heat is primarily due to the process of oxidation which is incessantly going on in the human economy. The temperature of the blood is not uniform throughout the body; that of the hepatic and portal veins has a higher temperature than ordinary venous blood, a state of things referable probably to more active local oxidation (see 'Functions of the Liver,' Chap. VIII.); the blood in the right ventricle is also warmer than that in the left one.

The difference between arterial and venous blood is slight as regards the composition; the former contains more water and fatty matter. But there is a more vital difference between the two, consisting in the different degree of oxidation—a state of the blood which depends upon the presence in it of the red colouring-matter (hæmato-crystalline), containing iron, of which more anon.

The coagulation of the blood which occurs after it has been removed from the body, and which sometimes happens in disease to a smaller extent during life, is a phenomenon not yet satisfactorily explained. It will be studied more in detail hereafter.

Besides the various albuminous matters present in blood, viz., fibrin, albumin, globulin, and the colouring-matter hæmato-crystalline, it contains oleic, stearic, lactic, hydrochloric, phosphoric, and sulphuric acids; these are more or less in combination with sodium, potassium, ammonium, calcium, and magnesium. The fat present in blood amounts to about 2 per cent., and it contains also soaps or saponified fats. The blood also contains a little cholesterine and a phosphorised body identical with one of many similar principles contained in the brain, but different from that apparently present in the bile. The blood also contains a little nitrogen in a dissolved state, and oxygen; but the oxygen is mainly held in a sort of combination with the colouring principle. Again, the carbonic acid given off at all points of the body is held in the blood partly in a dissolved state and partly as carbonate of sodium.

It is intended to study hereafter the chemical constitution of the corpuscles of blood, but it should be stated here, that beyond their own chemical constituents, a certain amount of a matter called stroma is present, and it is this which is supposed to give shape to the corpuscles. Stroma is not albuminous in nature, being soluble in ether, alcohol, and chloroform; but it contains a small amount of fibrino-plastic substance, termed paraglobulin by Schmidt.

The total amount of blood contained in the body varies with the time and each person, and is difficult to estimate, but ordinarily it appears to amount to about one-tenth of the body-weight. Bischoff has more recently determined the quantity at 7·7 per cent. of the weight of the body.

J. Steinberg[1] has determined the absolute mass of the blood in various animals, and he gives the following table showing the relative weights of the blood and of the bodies of the animals from which it was derived :—

Rabbits	1 : 12·3–13·3
Guinea pigs	1 : 12·0–12·3
Dogs	1 : 11·2–12·5
Puppies	1 : 16·2–17·8
Cats	1 : 10·4–11·9
Cats fasting	1 : 17·8
Kittens	1 : 17·3–18·4

According to Schmidt and Lehmann,[2] the following tables represent the composition of blood-corpuscles and liquor sanguinis, but how far these were perfectly separated from each other, and without prejudice to their relative compositions, it is difficult to state.

Specific gravity of blood corpuscles, 1·0885
1000 parts contain—

Water . . 688·00		
Solid constituents 312·00 containing	Hematin	16·75
„ „ „ „	Globulin and cell membrane	282·22
„ „ „ „	Fat	2·31
„ „ „ „	Extractive matters	2·60
„ „ „ „	Mineral substances	8·12
		312·00

The mineral matters include	Chlorine	1·686
„ „ „	Sulphuric oxide (SO_3)	0·066
„ „ „	Phosphoric anhydride (P_2O_5)	1·134
„ „ „	Potassium	3·328
„ „ „	Sodium	1·052
„ „ „	Oxygen	0·667
„ „ „	Calcic phosphate	0·114
„ „ „	Magnesic „	0·073
		8·120

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[1] Pflüger's *Archiv.* vii. 101–187.

[2] Miller's *Organic Chemistry*, 3rd Edit. p. 870.

Specific gravity of Liquor sanguinis 1·028
1000 parts contain—

Water	902·90				
Solid constituents	97·10 consisting of—				
		Fibrin	4·05		
	1000·00	Albumin	78·84		
		Fat	1·72		
		Extractive matter	3·94		
		Mineral substances	8·55 consisting of—		
				Chlorine	3·644
			97·10	Sulphuric oxide (SO_3)	0·115
				Phosphoric anhydride (P_2O_5)	0·191
				Potassium	0·323
				Sodium	3·341
				Oxygen	0·403
				Calcic phosphate	0·311
				Magnesic „	0·222
					8·550

We also take from the same source as that which furnishes the two foregoing tables, the next one, representing, according to Becquerel and Rodier, the average composition of blood in man and in woman :—

	Man.	Woman.
Specific gravity of defibrinated blood	1·0600	1·0575
Specific gravity of serum	1·0280	1·0274
Composition—		
Water	779·00	791·10
Fibrin	2·20	2·20
Serolin[1]	0·02	0·02
Phosphorised fat	0·49	0·46
Cholesterine	0·09	0·09
Saponified fat	1·00	1·05
Albumin	69·40	70·50
Blood corpuscles	141·10	127·20
Extractive matters	6·80	7·40
	1000·00	1000·00

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[1] This may be disregarded. It is a name given to a substance which has never been analysed, and it may be included in that with which it is probably identical, viz. fat, in some form or other.—AUTHOR.

	Man	Woman
Sodic chloride	3·10	3·90
Other soluble salts	2·50	2·90
Earthy phosphates	0·33	0·35
Iron in terms of metal	0·57	0·54
	6·50	7·69

The extractives consist of sugar, urea, kreatin, kreatinin, lactic acid, uric acid, hippuric acid, leucine, tyrosin, xanthine, and hypoxanthine.

G. Bunge has recently published[1] some interesting analyses of the blood of pigs, horses, and oxen, which we reproduce here.

I. Defibrinated Pig's Blood.

Per 1000 parts of blood corpuscles.		Per 1000 parts of serum.	
Water	632·1	Water	919·6
Solid constituents	367·9	Solid constituents	80·4
Hæmoglobin	261·0	Albumin	67·7
Albumin	86·1	Other organic substances	5·0
Other organic substances	12·0	Inorganic substances	7·7
Inorganic substances	8·9	Potash	0·273
Potash	5·543	Soda	4·272
Magnesia	0·158	Lime	0·136
Chlorine	1·504	Magnesia	0·038
Phosphoric acid	2·067	Oxide of iron	0·011
		Chlorine	3·611
		Phosphoric acid	0·188

II. Defibrinated Horse's Blood.

Per 1000 parts of blood corpuscles.		Per 1000 parts of serum.	
Water	608·9	Water	896·6
Solid constituents	391·1	Solid constituents	103·4
Potash	4·92	Potash	0.27
Chlorine	1·93	Soda	4·43
		Chlorine	3·75

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[1] *Zeitschrift f. Biologie*, xii. 191–216.

III. Defibrinated Ox Blood.

Per 1000 parts of blood corpuscles.	
Water	599·9
Solid constituents	400·1
Hæmoglobin	280·5
Albumin	107·3
Other organic substances	7·5
Inorganic substances	4·8
Potash	0·747
Soda	2·093
Magnesia	0·017
Chlorine	1·635
Phosphoric acid	0·703

Per 1000 parts of serum.	
Water	913·3
Solid constituents	86·7
Albumin	73·2
Other organic substances	5·6
Inorganic substances	7·9
Potash	0·254
Soda	4.351
Lime	0·126
Magnesia	0·045
Oxide of iron	0·011
Chlorine	3·717
Phosphoric acid	0·266

The liquor sanguinis means serum holding fibrin in solution; serum being that part of the blood which is left when the fibrin, enclosing in its meshes the corpuscles, has been separated by spontaneous coagulation. The serum produced by whipping blood is a less perfect one, inasmuch as it contains more corpuscles than the former one. The mixture of fibrin and corpuscles which forms on spontaneous coagulation is often named *cruor* or *crassamentum*.

The serum produced in this last-mentioned process is a straw or faintly-red coloured transparent liquid, exceedingly liable to putrefaction. Its composition is tolerably well expressed by the tables given above, after deducting the fibrin included in the liquor sanguinis. Among its albuminous constituents exists paraglobulin, fibrinogeneous matter, and some sodium-albumin or serum-casein, as it has been designated, and a little potassium-albumin. Seralbumin proper, however, enters most largely into its albuminous constituents; while fibrin, which is a more complicated body than albumin, is supposed to be produced in coagulation (Schmidt) by the action of paraglobulin upon fibrinogeneous substance.

Blood in life contains rather less than half its own volume of gaseous matter, consisting of oxygen, carbonic acid, and nitrogen.

Of the Sugar present in Blood.—That sugar is a normal constituent of blood might be inferred from a knowledge of the various processes occurring in the digestive apparatus, which result in the transformation of starchy matters into sugar. For the detection of this principle in the blood there are several methods more or less reliable.

One recommended by Bernard consists in making the blood into a paste with animal charcoal, addition of a little water, and filtration. The filtrate should be colourless, and Trommer's test for sugar may be then applied to it.

In another method, the blood is precipitated with much alcohol, and the precipitate extracted with tolerably strong spirit; from the combined solutions the alcohol is distilled off, and the residual watery solution tested for sugar. Both these methods remove albumin and colouring matter, and some other matters which might interfere with tests for sugar.

Moore's test is only reliable when the sugar is present in considerable amount; it consists in boiling a solution (after applying one of the two foregoing methods to blood) with strong potash or soda, when the presence of sugar is revealed by a colour which is first yellow, then reddish, and finally black or brown.

Böttcher's test consists in the addition of a pinch of oxide of bismuth or its subnitrate to the suspected solution, previously rendered alkaline by a large excess of potash or soda. The fluid, in the presence of sugar, becomes black or dark grey on boiling, owing to the reduction of the bismuth.

The fermentation test for sugar is well known. A given quantity of solution is maintained in a suitable vessel at 35° C. in contact with a little yeast. Any carbonic anhydride which is evolved may be caught in baryta water, and the precipitate of baric carbonate afterwards isolated, dried at 100°, and weighed; while the alcohol, if any be produced in the solution, may be distilled off, made up to the original volume of the solution employed, and its specific gravity taken. By these means the amount of sugar may be estimated. The alcohol may be detected qualitatively by adding a little potassic bichromate solution acidified by sulphuric acid, and boiling; alcohol turns the solution green by reduction. Sugar may be estimated by the ordinary process, which consists in the reduction of a standard Fehling's solution, or by boiling with excess of Fehling's solution, and isolating the cuprous oxide thus formed, converting it into cupric oxide by ignition and weighing.

Amount of Sugar present in Blood.—From the determinations made by Lehmann and Dupré, the percentage of sugar present in normal healthy blood is extremely small, and generally amounts to 0·04 per cent. only.

In a recent paper,[1] C. Bernard shows that sugar is a vital constituent of blood, and exists in quantities varying from 1 to 3 parts per 1000. It rapidly disappears from the blood after death, and so also from blood which has been withdrawn from the body. Thus Bernard found in the blood of a dog as much as 1·07 parts per 1000, immediately after drawing it from the body, but after standing five hours it had diminished to 0·44 parts per 1000, and after twenty-four hours it had totally disappeared. Bernard also shows that arterial blood contains more sugar than venous blood, as the following results indicate.

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[1] *Ann. Chem. Phys.* [5], ix. 207–258.

	Sugar per 1000 parts.	
	Arterial Blood.	Venous Blood.
Dog (i)	1·45	0·73
„ (ii)	1·24	0·99
„ (iii)	1·17	0·88

Finally, Bernard claims to have traced the production of the sugar found in blood to the liver, but of this part of the subject we have already treated.

Since the publication of Bernard's paper, Dr. Pavy has communicated[1] to the Royal Society two papers relating to the sugar found in blood and its determination. His method consists in properly preparing the blood by coagulation, filtration, &c., and then boiling the solution with excess of potassio-tartrate of copper. The suboxide of copper thus obtained is oxidised by a few drops of peroxide of hydrogen, dissolved in nitric acid, and from this solution the copper is electrolytically deposited on a platinum spiral and weighed. It is only the application of this method that Dr. Pavy can claim as new, and indeed barely that, inasmuch as chemists have long been acquainted, and have used every particular in this method. Pavy then claims to have demonstrated that—

1000 parts of dog's blood contains an average of 0·787 parts sugar.
1000 „ sheep's „ „ „ 0·521 „ „
1000 „ bullock's „ „ „ 0·543 „ „

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[1] June 14 and 21, 1877.

He contrasts these results with those obtained by Bernard and described above, and also states that he has observed no difference in the amount of sugar present in arterial and venous blood; but he agrees with Bernard on the diminution and ultimate entire disappearance of the sugar in blood, after death or after withdrawal from the body.

It is not possible to decide whether Bernard or Pavy is right in the matters where they disagree, until more work of a chemico-mathematical order shall be forthcoming.

Blood Corpuscles and their Chemical Constitution.—The corpuscles of the blood are of a twofold character, viz., red and colourless, but the latter, while larger in size, are far less numerous than the former.

The red corpuscles are flattened circular disks, having an average diameter of $\frac{1}{3200}$ of an inch, and a thickness of about one-fourth of this. From this it follows that more than 10,000,000 will cover only one square inch, and it has been calculated that a cubic inch of blood contains no fewer than 70,000,000,000 corpuscles. The colourless corpuscles have an average diameter of $\frac{1}{2500}$ of an inch.

The red corpuscles are soft, flexible, and elastic bodies, and are semifluid in the centre, where globulin is held in solution; they derive their colour from a special substance found nowhere else in the body. By exposure to carbonic anhydride, the red corpuscles swell out, while oxygen flattens them.

Colourless corpuscles are constantly vibrating; 'undergoing active contraction, or being passively dilated by the contraction of other parts.'[1]

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[1] Huxley, *Lessons in Elementary Physiology*, p. 63.

It appears certain that the red corpuscles are in some way or the other derived from the colourless ones, but the exact changes and steps have not been ascertained; even the origin of the colourless ones is not known, although it is supposed that they are formed in the ductless glands, and pass as lymph corpuscles into the blood. The colourless corpuscles increase in number after eating, and diminish between the meals.

The corpuscles of blood, which are heavier than the plasma, are best isolated by treating defibrinated (by whipping) blood with its own volume of a solution of common salt consisting of a saturated solution diluted ten times. The mixture is stirred, and then put on one side to settle; when the corpuscles have deposited, the supernatant liquor is decanted, and the deposit washed by decantation with a similar solution of salt, and in this way the corpuscles are obtained free from serum. They consist of stroma or colourless skeleton containing hæmatocrystalline (hæmaglobulin), a little cholesterine, a phosphorised body, paraglobulin, and salts consisting chiefly of potassic chloride and sodic phosphate. The stroma is insoluble in water and salt, but easily soluble in ether, chloroform, and alkalies; so that, when washed corpuscles are shaken up with water and ether, the stroma, cholesterine, and fatty matters are taken up by the ether, while the colouring matter of the blood is liberated and dissolves in the water. The filtered aqueous solution crystallises on exposure to a temperature of $-5°$ to $-10°$ C., but sometimes it is necessary (for instance, when the blood is from birds) to add alcohol before crystallisation ensues. The deposit from the blood of man, the ox, and sheep is, however, amorphous, but in every case it consists of hæmatocrystalline. The cholesterine may be extracted from the corpuscles separated from the blood as described, by means of alcohol; it is easily recognised, and is accompanied by a phosphorised body. Hoppe-Seyler has estimated that the corpuscles present in 100 cc. of blood contain 0·04 to 0·06 grm. cholesterine. Blood-crystals from man consist of four-sided prisms with dihedral summits, and when from other animals they are also of a rhombic character, but the precise form differs.

These crystals contain 0·43 per cent. iron, and analyses invariably lead to an atomic weight for the molecule of 13,280, and to the formula $C_{600}H_{960}FeN_{154}S_3O_{177}$. Hæmatocrystalline is insoluble in alcohol, chloroform, ether, benzene, and other solvents, but readily soluble in water and alkaline solutions. Notwithstanding the large size of the molecule of hæmatocrystalline, there appears to be little doubt of its individuality, inasmuch as the percentage of iron is a constant, and its other properties confirm the fact. It contains, therefore, or consists of the following proximate principles: an albuminous substance which, when separated, is amorphous and colourless, and a crystalline body named hematine. Of the first of the substances nothing is known, but many researches have been made relative to the second. To obtain it in a crude state, the process of Wittich is most applicable, and this consists in treating blood with seven times its bulk of a cold solution of potassic carbonate, containing one part by weight of the salt in two parts of water. The mixture is filtered through calico, then pressed and afterwards heated with alcohol to free it from the excess of potassic carbonate, and then dried. It is now extracted with alcohol at 40° C., and the extracts are treated with an equal volume of absolute alcohol containing tartaric acid in solution. In this way the potash is precipitated, and the hemine remains dissolved, but is precipitated on cooling (after concentration of the filtrate) in minute bluish black crystals consisting of rhombic plates.

Thudichum and Kingzett[1] have analysed these crystals and obtained from them their proximate constituents, for as thus isolated they are not constituted of one individual substance.

Synopsis of Analyses.

	(*a*)	(*b*)	(*c*)
Iron	7·677	7·625	
Chlorine	2·98	3·08	3·005
Phosphorus	0·6666	0·5105	0·6479

Now hemine, as this substance is termed, has been considered as a hydrochloride of hematine, but these analyses of a perfectly crystalline substance show that the substance cannot be regarded as a chemical individual, but as a mixture of two or several matters.

From the fact of its taking up hydrochloric acid when exposed to a current of that gas, it is seen that 'hemine' must contain free hematine. Preyer in his treatise on blood-crystals states that hemine dissolves in nitric acid with decomposition, and that ammonia throws down white hydrated ferrous oxide from the yellowish solution. This statement, in itself incredible, because ferrous oxide cannot exist in a nitric acid solution, is shown by Thudichum and Kingzett to be incorrect in its entirety. Preyer must have mistaken the precipitate yielded by mere dilution of the nitric acid solution for one yielded by ammonia, because the precipitate is entirely soluble in excess of ammonia and contains the original amount of iron.

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[1] On Hemine, Hematine, and a Phosphorised Substance contained in Blood Corpuscles. *Journ. Chem. Soc.*, September 1876.

C. Paquelin and L. Jolly,[1] in a paper on the colouring matter of blood, have stated that it does not contain iron. In former papers they claimed to have demonstrated that the iron present in blood corpuscles exists as tribasic ferrous phosphate, and in the paper cited they undertake to substantiate their former proposition.

Thudichum and Kingzett have repeated the experiment of Paquelin and Jolly, but with no confirmation of their results. The errors of the French chemists are made perfectly manifest, and other important results are established. Thus it is shown that by acting upon hemine with a mixture of acetic and citric acids under the conditions stated by Paquelin and Jolly, its composition is not affected ; but by extracting it with benzene and acetic acid, a certain amount of hematine goes into solution, while the larger quantity remains undissolved, and is freed from the phosphorised impurity by means of the benzene which dissolves the latter. The undissolved portion in fact proved to be probably the purest hematine ever made, and gave on analysis the formula $C_{32}H_{32}FeN_4O_6$. The benzene and acetic acid extracts, after freeing from benzene by distillation, left a black viscous matter which proved mostly soluble in hot absolute alcohol, and deposited therefrom on cooling in a perfectly white form. Its alcoholic solution gave combinations with platinum chloride, cadmic chloride, and lead. The cadmic chloride salt was recrystallised from alcohol and analysed, when the fact of its identity with one of the phosphorised constituents of brain-matter was established. This is shown by the following comparison of the analytical figures.

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[1] *Compt. Rend.* 79 (1874), 918.

	Phosphorised Principle from Blood Corpuscles	Phosphorised Principle from Brain[1]
C.	64·90	64·66
H.	11·65	11·30
N.	3·30	3·11
P.	4·42	4·15
O.	15·72	16·78

The cadmic chloride compound gave the formula $C_{76}H_{164}N_3P_2O_{14}.2(CdCl_2)$.

This is the first time that the isolation and analysis of any definite phosphorised principle of the blood has been effected; at the same time the method of isolation would not preclude the presence of yet other similar compounds (see 'Brain Chemistry' hereafter).

To return to the consideration of hematine, it will be seen that the formula of Thudichum and Kingzett is $C_{32}H_{32}FeN_4O_6$. Hoppe-Seyler, after abandoning several varieties of formulæ, now gives $C_{34}H_{34}N_4FeO_5$, but the afore-named chemists, in a criticism of his analytical results, show that this formula is not absolutely trustworthy. Thus he found an excess of nitrogen for his theory, and explained it as due to an absorption of ammonia from the air while washing on a filter. This could not be, for so sensitive is hematine to ammonia, that the presence of mere vestiges in the air causes hematine at once to dissolve and to pass through the filter. It is revealed by its colour, and may be reprecipitated by a trace of acetic acid.

The colouring-matter of the blood has had assigned to it so many names, as also those proximate principles which are derived from it as described, that it will be best to present the facts in a form which will enable the memory to retain a true regard of their position.

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[1] *Report Medical Officer of the Privy Council*, &c., New Series, No. iii. (1874), 174.

Hæmatocrystalline or hæmoglobulin is the colouring matter of the blood; the formula for it is $C_{600}H_{960}FeN_{154}S_3O_{177}$. This consists of hematine and albuminous matters. From the blood there may be obtained hemine, a substance primarily consisting of hematine, but containing also hydrochloride of hematine and a phosphorised principle. When hemine is submitted to the process described by Thudichum and Kingzett, pure hematine is obtained from it of the formula $C_{32}H_{32}FeN_4O_6$, and the phosphorised principle is isolated in a pure state, and found to be identical with one present in brain-matter.

General Characters of Hematine.—Hematine is insoluble in water; it is also insoluble in ether when neutral, and but slightly soluble in alcohol. It readily dissolves in caustic alkalies, particularly ammonia, and also in acid or alkaline alcohol.

Hoppe-Seyler has assigned the name hæmato-popphyrin to a substance said to be free from iron and obtainable from hematine by treatment with strong sulphuric acid, but no proof of this fact has ever been presented, that is to say it has never been shown by analyses that the preparation is free from iron. The same author also states[1] that by the action of tin and hydrochloric acid and other reducing agents upon an alcoholic solution of hematine, a yellow colouring matter is obtained agreeing in properties with the urobilin of Jaffe and the hydrobilirubin of Maly. Hoppe-Seyler heads his paper 'Formation of the Colouring-matter of

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[1] *Deut. Chem. Ges. Ber.* vii. 1065.

Urine from Blood,' but for such a title there is no justification. The urobilin of Jaffe is a mixture and has never been analysed; the hydrobilirubin of Maly, whatever it may be, is not yet established; Hoppe-Seyler gives no analysis of his product. Indeed, in regard to the many mere statements made of late years by various authors relative to the assumed identity of colouring-matters present in the blood, the bile, and the urine, it may be said with all justice that such identity has not received a single analysis in its favour or a single proof of its truth. It is for similar reasons that many papers bearing on physiological chemistry, but totally unsupported by analytical data, are not noticed in this work.

A. Béchamp,[1] for instance, has described a process for obtaining hematine in a pure and soluble form, but that his product is pure is not sustained by any analytical or other evidence. Defibrinated blood is mixed with water and precipitated by lead acetate, and basic lead acetate containing 10 per cent. of solution of ammonia, successively. The filtrate, yet containing the blood pigment, is freed from lead by carbonic anhydride or carbonate of ammonium, and dried at 35° to 40°. The garnet-coloured laminæ contain a little ammonium carbonate, acetates of the alkalies, and probably urea. To free from these, the red solution after the basic lead precipitate, is mixed with half its volume of 50 per cent. alcohol, and is then again precipitated with ammoniacal lead acetate. The brick-red precipitate is isolated, washed with 40 per cent. alcohol (out of contact with carbonic anhydride), mixed with water, a little ammonic carbonate added, and then decomposed by means of carbon dioxide; the filtered solution coagulates at 61°, and must be dried below that temperature to obtain the 'pure solid pigment.' But what is meant by 'the pure solid pigment,' and what it is, is not shown.

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[1] *Ann. Chim. Phys.* (5) iii. 340–342.

Alex. Schmidt[1] asserts that the colouring-matter of the blood has nothing to do with its coagulation, but that this has its source entirely in the protoplasm. Hematine and hæmato-crystalline occur in the urine in cruenturesis (paroxysmal hæmaturia); while a diminution of hæmatocrystalline in the blood constitutes the disease termed 'chlorosis' or 'anæmia.'

The Coagulation of Blood.—Of all the properties exhibited by blood, the most remarkable, perhaps, is its power of coagulation. This act generally sets in after the blood has been removed from the body, in from four to five minutes, but it is retarded by exposure to a low temperature, and when kept at 0° will not coagulate at all; it is accelerated by an increase in temperature, taking place most readily at about 38° C. The coagulation is prevented by allowing the blood to flow from the vein into alkaline solutions, or concentrated solutions of various salts, such as potassic nitrate or sulphate and acetate of sodium. In certain cases of sudden death, the blood also appears to lack its power of spontaneous coagulation.

Contact of the blood, as it is withdrawn from the body, with non-living matter promotes coagulation, while direct contact of living matter retards or entirely prevents its coagulation. Thus, if it be kept in a portion of a vein tied at both ends, it remains fluid for a long time. Still more remarkable is the fact that blood not only is not coagulated when poured into the excised heart of a turtle, but solidified blood becomes fluid again under these conditions and remains so, as long as the heart lives, which it does for some hours or days after excision. The living surfaces of blood-vessels are therefore the agencies which preserve the fluidity of the blood; but as yet we do not even know the *rationale* of the process of coagulation.

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[1] Pflüger's *Archiv. f. Phys.* ix. 353–357.

It is certainly known that when blood is allowed to stand it becomes solid, and the solid matter thus coagulated encloses in its meshes the blood-corpuscles. The same solid substance is obtained by whipping the newly-drawn blood, and may be obtained white by washing with water to free it from blood-corpuscles. This substance is called fibrin, and fibrin appears to be a more complex substance than seralbumin, since, on the one hand, it seems to be elaborated from albumin, and on the other hand, to yield that substance under certain slight decomposing influences. But what is not yet decided is this: has the fibrin existed previously in the blood in a state of solution, or is it a synthetical product under changed conditions? The most acceptable explanation of the coagulation of the blood originated with Alex. Schmidt. He supposes that blood contains two substances, viz., fibrino-plastic substance or paraglobulin, contained in the serum and corpuscles, and fibrinogen also contained in the serum and other fluids of the body; he further supposes that these two substances have the power of combining to form fibrin. Now it is quite true that in a sense such substances may be isolated and behave as indicated when they are brought together.

The globulin or paraglobulin of blood-corpuscles, when added to serous infusions (such as hydrocele fluid or fluid of pericardial, pleural, or peritoneal exudation) developes fibrin. It does so chiefly in a weakly alkaline solution; strong acids and alkalies completely suspend its action, but it does not lose its power by drying or keeping in alcohol. The substance contained in the serous infusions, and upon which the paraglobulin acts, may also be isolated; but what is yet wanted before this hypothesis of the cause of coagulation of blood can be accepted, is the establishment of accurate formulæ for the two substances supposed to be concerned, and the further proof of their combination in molecular proportions. It is possible that the paraglobulin acts as a ferment by contact action, but whatever be the explanation, another explanation must be provided to show why coagulation does not occur in the living blood-vessels.

In another paper,[1] A. Schmidt claims to demonstrate that the colourless corpuscles of the blood constitute the true source of fibrin ferment, or rather that they become so as soon as the blood has left the body; at the same time he states that coagulation is attended with the destruction of white corpuscles. In a yet later paper[2] it is stated that the ferment is present in all cells which contain protoplasm; these include lymph, chyle, and pus cells, and perhaps connective tissue generally. The same author has also given further information regarding the coagulation of fibrin in yet another paper.[3] But in opposition to these views, Olof Hammersten[4] contends that paraglobulin does not unite with fibrinogen to form fibrin, nor become in any way converted into fibrin. He gives experiments in support of his views, but it is quite unnecessary to consider them at all in detail, for the reason why we have so briefly condensed other papers bearing upon the subject of coagulation, viz., that the authors have dealt with substances which cannot be defined by analytical figures, and that chemico-mathematical considerations are not included in their researches; so that it is never known what it is precisely they have experimented upon, nor is it possible to place a fair interpretation upon their views, except in the most general manner. We must now give some attention to a more recent view of the causes of the coagulation of blood.

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[1] Pflüger's *Archiv. f. Phys.* xi. 515–577. [2] *Compt. Rend.* lxxxiv. 78-80.

[3] *Compt. Rend.* lxxxiv. 112–115.

[4] Pflüger's *Archiv. f. Phys.* xiv. 211–273.

E. Mathieu and V. Urbain have stated[1] (in 1873), that when egg albumin is deprived of the carbonic anhydride it contains, by means of the exhaust (mercury) pump, it also loses certain volatile salts, viz., ammonium carbonate, and traces of sulphate and sulphide, and that in this condition it is not coagulable even at 100°; the deprivation of albumin of its salts they state to convert it into globulin. These statements, in themselves utterly inacceptable to chemists, were reiterated[2] in a subsequent paper, and while it was again stated that the cause of the coagulation of blood is the presence of carbonic acid, it was said that this latter may be removed by exosmose, and that its effects may be neutralised by neutralisation with an alkali.

In opposition to these views, A. Gautier[3] made a

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[1] *Compt. Rend.* lxxvii. 706–709.

[2] *Journ. Pharm. Chim.* (4) xx. 337–345.

[3] *Compt. Rend.* lxxx. 1360–1363.

number of experiments confirmative of the view that the death of the blood is essential for coagulation, and disproving the hypothesis of Mathieu and Urbain. It may here be stated also that on the publication of these papers, Dr. Thudichum, in conjunction with the author of this work, made a number of experiments, and repeated those of Mathieu and Urbain, and it appeared from these that the new view of the causes regulating the coagulation of blood was utterly without foundation. M. F. Glénard also described[1] experiments to the same effect. To this latter chemist, Mathieu and Urbain replied,[2] describing a few experiments in which it was demonstrated that exposure to carbonic anhydride determined the coagulation of the blood, even when kept in contact with the segment of a blood-vessel. The best answer, however, to these experiments, is the fact that blood does not coagulate in life under conditions where carbonic acid is certainly present in the blood-system. To sum up these observations, it may be admitted that so far, no perfectly acceptable explanation has been given of the cause of the coagulation of blood.

The Albuminous Principles contained in Blood.—The serum of the blood contains, as already stated, a modification of albumin termed seralbumin; this is present to the extent of 7 to 9 per cent. in the serum, which also contains a small amount of paraglobulin. It also contains sodium-albumin and a little potassium-albumin.

The paraglobulin, or fibrino-plastic substance, may be precipitated from serum, after dilution with ten volumes of water by means of carbonic anhydride; while the alkaline albuminates are precipitated on addition of a little acetic acid.

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[1] *Compt. Rend.* lxxxi. 102–103. [2] *Ibid.* 535–536.

Seralbumin is completely precipitated by boiling in the presence of a little acetic acid also, but if no acetic acid be present, sodium-albumin remains dissolved.

The fibrinogenous matter of the serum is deposited in an adhesive form, after removal of the paraglobulin, by dilution and exact neutralisation with acetic acid.

Fibrin produced by spontaneous coagulation or whipping of blood is supposed to result from the action of paraglobulin upon fibrinogenous matter. Fibrin is characterised by certain definite properties which are easily demonstrated.

Thus if it be kept moist and in a warm place, it gradually liquefies (Liebig) and decomposes after the manner of putrefaction, evolving butyrate and valerate of ammonium; but the most remarkable fact is, that albumin appears to be produced, and may be identified by its coagulable and other properties. Ammonic sulphide is also formed.

Its ultimate products of decomposition are similar to those of albumin.

Fibrin dissolves in dilute caustic potash at 60° C., and in the filtrate, acetic and phosphoric acids produce precipitates soluble in excess of the acid.

If boiled with caustic potash, fibrin evolves ammonia, and potassic sulphide is formed in the solution.

Concentrated hydrochloric acid, aided by warming, dissolves fibrin to a violet-coloured solution: nitric acid turns it yellow and dissolves it.

Tannic acid precipitates it from its solutions, and peroxide of hydrogen is decomposed by it; this latter property is particularly distinctive.

The Blood in Disease.—The blood presents an expression of the whole state of the body; combining in one the elements of nutrition and excrementation (to some extent), and presenting the powers which enable the greatest process of life, viz., respiration, to be carried on. It is the feed-stream and the sewage-system at once of the human economy, and hence its composition is affected by every change in health or disease.

Thus in fevers, cholera, diarrhœa, and the like diseases, the amount of water in the blood is diminished, from the fact that a greater wearing down of the solid tissues is experienced; in gout, uric acid occurs as urates of sodium and calcium; in diabetes, the amount of sugar present is abnormally high; in jaundice, biliary colouring matters are found present; while formic acid occurs in leukocythæmia.

In certain diseases, Thudichum has found free fatty acid in the blood, emulged by the sodium phosphate which it contains.

Thudichum has also shown, in a research upon cholera (published in the 'Reports of the Medical Officer of the Privy Council'), that in this disease, the serum of the blood exhausts water and other matters from the blood-corpuscles, which latter henceforth cease to be carriers of oxygen.

In yellow fever some of the colouring-matter of the blood decomposes and colours the skin yellow; while in paroxysmal cruenturesis it appears in the urine as a red matter. In cases of poisoning by arseniuretted hydrogen, serpents' bites, or sulphuretted hydrogen, prussic acid, ammonia, &c., the colouring matter of the blood is also seriously affected, but in what precise manner is unknown.

CHAPTER X.

NUTRITION OR ALIMENTATION.

The processes of life are sustained and kept in order by means of the food which we take into our mouths, and which is prepared for assimilation by the various processes of digestion already studied. The chyle is the fluid by means of which the blood is kept constantly supplied with new matter, to be afterwards absorbed by the body in place of those parts broken down by every act of life. In this way a man of average size and activity must take into his body 8,000 grains of chemically dry solid matter, if he is not to gain or lose in body weight. The blood also absorbs through the lungs about 10,000 grains of oxygen, making a total daily gain of 18,000 grains, or nearly 2¾ lbs. avoirdupois of solid and gaseous matter.[1] The alimentary canal excretes not more than 800 grains of dry solid matter in the same period, and it therefore follows that 7,200 grains of solid matter must pass out of the body in other forms as well as the 10,000 grains of oxygen. These 17,200 grains of matter pass out of the body through the breath, the sweat, and urine. Of course the matters which leave the body are not identical in nature with those substances absorbed in the body, but they constitute the effete changed substances resulting from the metamorphosis of animal tissue. Food therefore is substance which, when introduced into the body, and modified by the processes of digestion, serves for the renewal of body structure, or for maintaining vital action. Some foods, being nearly identical in nature with some of the substances entering into the constitution of the tissues, require but little change before being capable of assimilation. Other foods are not assimilated in the sense that their substance is taken up by, and becomes part of the tissues, but serve other functions equally important. No one food serves to supply all the materials required by the body, but they differ in value according to the degree in which they supply one or more requirements.

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[1] Huxley's *Elements of Physiology*, p. 138, 1st edit.

The mass of the body consists of various forms of albuminous principles; these are built up in the body by a re-arrangement of allied principles taken in the food. The fat which we eat is not supposed to give rise to the whole amount of fat in the living tissue, but is what is termed a respiratory food, being oxidized in the blood —an act which is attended with the generation of force, ordinarily viewed as heat, but not necessarily so. The fat present in the body tissues is supposed to be derived in some way from saccharine food, and in part from albuminous substances. In experiments made by Gundelach and others, it was found that bees fed exclusively upon sugar secreted wax in abundance; about 20 lbs. of sugar being consumed while 1 lb. of wax was being produced.

The principles of the brain and nervous system appear to be built up, at least for the most part, by synthetical processes occurring in the body, but otherwise unknown at present. The various secretions of the body are produced by acts of decomposition which will receive special consideration hereafter. Everywhere in the animal economy mineral matters are found either in the free state or associated in combination with organic principles. The bones and teeth in particular contain a large proportion of earthy matters, and hence it is necessary that our food should include matters from which a proper supply of these substances is obtainable.

The nitrogenous parts of the body are in the main derived directly or indirectly from the vegetable kingdom (as elsewhere pointed out), and in a large measure therefore the vegetable is constructive, while the animal is both constructive and destructive.

While life may be maintained for a greater or less length of time by a restricted number of kinds of food, perfect health and unimpaired functions are best secured and maintained upon a mixed diet comprising all the matters—nitrogenous, saccharine, amyloid, and saline—which are available for sustenance. The idea of food is too often identified with solid matters of which we partake, but in truth, air and water are as necessary foods as any others. Moreover, there are many kinds of food which, while they are not absolutely necessary, are not therefore harmful when partaken of in proper amount; these may be considered as luxuries, but they are nevertheless foods. Among this class of bodies we have alcohol, which must be placed side by side with fat as a respiratory food, or a substance which admits of oxidation in the lungs.

Every act of life, be it one of thought, will, consciousness, or work, is attended by the consumption of matter in the body. That is to say, all work done signifies something destroyed or changed. It is difficult to decide in many cases whether these changes—generally of oxidation—take place in the tissues themselves or in the blood; but be it one or the other, the same necessity exists for food, which must take the place of matter used up in previous acts of life. This is as essential to life as is the supply of oil to a lamp which is required to give light.

Starch and sugar are substances which require a deal of oxygen to burn them into carbonic anhydride and water.

$$C_6H_{10}O_5 + O_{12} = 6CO_2 + 5H_2O$$
$$C_{12}H_{22}O_{11} + O_{24} = 12CO_2 + 11H_2O$$

It will be seen from these equations that starch and sugar contain in themselves sufficient oxygen to burn their hydrogen into water, but that required by the carbon is supplied in the lungs from the air inspired. Fats, however, require far more oxygen than starch and sugar, because they do not contain even enough oxygen for the combustion of the hydrogen present in them. So also with the fatty acids into which and glycerine, fats are resolved (at least in part) in the processes of digestion. This may be instanced with stearic acid derived from the tristearine of mutton fat.

$$C_{18}H_{36}O_2 + O_{52} = 18CO_2 + 18H_2O$$

From the fact that oxidation in the lungs is a process of combustion, and the source of muscular power, the foods which undergo this process are termed heat producers; but we shall see presently that it is by no means clear that blood oxidation is attended directly with the evolution of animal heat.

In his work on 'Practical Hygiene,' Parkes quotes the figures of Moleschott in illustration of the amount of food required by an adult man of average weight—140 lbs. —who occupies himself in moderate work. These are as follows :—

Dry Food.	Ounces.	Grains of Nitrogen.	Grains of Carbon.
Albuminous substance	4·587	317	1073·6
Fatty "	2·964	nil	1024·4
Carbohydrates	14·257	"	2769·4
Salts	1·058	"	
	22·866		

With this knowledge it is easy to calculate the dietary values of different kinds of food from their ascertained composition. The following table for calculating diets is taken from Hassall's work on Food.[1]

Food	Water	Albuminates	Fats	Carbohydrates	Salts
Raw lean meat	75	15	8·4	—	1·6
Fattened meat	63	14	19	—	3·7
Roast meats (including dripping)	54	27·6	15·45	—	2·95
Bread	40	8	1·5	49·2	1·3
Flour	15	11	2	70·3	1·7
Biscuit	8	15·6	1·3	73·4	1.7
Rice	10	5	0·8	83·2	0·5
Oatmeal	12	16	6·8	63·2	2·0
Maize	13·5	10	6·7	64·5	1·4
Dry peas	15	22	2	53	2·4
Potatoes	74	1·5	0·1	23·4	1
Carrots (no cellulose included)	85	0·6	0·25	8·4	0·7
Cabbage	91	0·2	0·5	5·8	0·7
Butter	8·8	2·7	85	—	3·5
Eggs (less shell)	73 5	13·5	11·6	—	1·0
Cheese	36·8	33·5	24·3	—	5·4
Milk of specific gravity 1030	86·7	4	3·7	5	0 6
Sugar	3	—	—	96·5	0·5

Dr. Hassall describes the use of this table as follows :—'The quantity by weight of any of the articles enumerated being known, the amounts of the albuminates, fats, and carbohydrates are easily calculated by a simple rule-of-three sum. Thus, supposing the allowance is 12 oz. of meat, one-fifth must be deducted for bone; the water in remaining 9·6 oz. will be ascertained as follows:

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[1] The table is, however, mainly taken from Dr. Parkes' work.

$$\frac{75 \times 9{\cdot}6}{100} = 7{\cdot}2\,;$$

and so on for the other constituents.'

Food, then, serves two main purposes: (*a*) to keep up the supply of force which may be registered, and is generally spoken of, as animal heat; and (*b*) to restore matter lost to the body by acts of life.

The following table[1] shows the amount of heat generated from ten grains of certain different foods during their complete combustion within the body. The figures themselves were worked out by Frankland, to whose experiments we shall further allude hereafter:—

Food.	In combustion raises lbs. of water 1° Fahrenheit.	Which is equal to lifting lbs. 1 foot high.
10 grains dry flesh	13·12	10,128
" " " albumin	12·85	9,920
" " " lump sugar	8·61	6,647
" " " arrowroot	10·06	7,766
" " " butter	18·68	14,421
" " " beef-fat	20·91	16,142

During sleep the vital action is low and tolerably uniform, but after partaking of food it is high and variable. As the amount of vital change proceeding in the body may be greater at some times than at others, it necessarily follows that a proportionate quantity of food will be required.

The next table, which is also taken from Ed. Smith's work 'On Foods,' shows the relative amount of air inspired during varying degrees of exertion :—

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[1] Taken from Edward Smith's work on Foods. H. S. King & Co., 1873.

The lying posture	being	1
„ sitting „	is	1·18
Reading aloud or singing	„	1·26
The standing posture	„	1·33
Railway travelling 1st class	„	1·40
„ „ 2nd „	„	1·5
„ „ upon the engine at 20 to 30 miles per hour	„	1·52
Railway travelling upon the engine at 50 to 60 miles per hour	„	1·55
Railway travelling in 3rd class	„	1·58
„ „ upon engine, average of all speeds	„	1·58
Railway travelling upon engine at 40 to 50 miles per hour	„	1·61
Railway travelling upon engine at 30 to 40 miles per hour	„	1·64
Walking in the sea	„	1·65
„ on land at 1 mile per hour	„	1·9
Riding on horseback at the walking pace	„	2·2
Walking at 2 miles per hour	„	2·76
Riding on horseback at the cantering pace	„	3·16
Walking at 3 miles per hour	„	3·22
Riding moderately	„	3·33
Descending steps at 640 yards' perpendicular per hour	„	3·43
Walking at 3 miles per hour and carrying 34 lbs.	„	3·5
Walking at 3 miles per hour and carrying 62 lbs.	„	3·84
Riding on horseback at the trotting pace	„	4·05
Swimming at good speed	„	4·33
Ascending steps at 640 yards' perpendicular per hour	„	4·4
Walking at 3 miles per hour and carrying 118 lbs.	„	4·75
Walking at 4 miles per hour	„	5·0
The tread-wheel, ascending 45 steps per minute	„	5·5
Running at 6 miles per hour	„	7·0

From the same series of experiments Smith determined the same effect, by showing the amount of carbonic acid evolved by respiration per minute :—

In profound sleep, lying posture	4·5	grains
In light sleep	4·99	”
Scarcely awake, 1½ A.M.	5·7	”
” ” 2½ ”	5·94	”
” ” 6¼ ”	6·1	”
Walking at 2 miles per hour	18·1	”
” 3 ” ” ”	28·83	”
Tread-wheel, ascending 28·15 feet per minute	43·36	”

The necessity for constantly renewing the protein matter, arises from the fact that the excretion of urea and other nitrogenous decomposition products of albumin is an ever-occurring process during life, no matter how extreme the inactivity. Indeed, protein, or flesh-forming food, is the only one absolutely necessary, in addition to mineral salts, for the continuation of life, inasmuch as it contains plenty of carbon and hydrogen to support animal heat also; but, for reasons to be immediately considered, it is better to take a mixed diet. If the food supply be deficient in nitrogen, the body begins to undergo a process of starvation—nitrogen starvation; and in such case the body feeds upon its own tissues until the failure of this supply and the action of induced secondary causes, puts a stop to life.

The advisability of a mixed diet is well stated by Huxley[1] as follows: 'A healthy full-grown man, keeping up his weight and heat, and taking a fair amount of exercise, eliminates 4,000 grains of carbon to only 300 grains of nitrogen, or, roughly, only needs one-thirteenth as much nitrogen as carbon. However, if he is to get his 4,000 grains of carbon out of albumin, he must eat 7,547 grains of that substance. But 7,547 grains of albumin contain, 1,132 grains of nitrogen, or nearly four times as much as he wants. Thus a man confined to a purely proteid diet must eat a prodigious quantity of it. This not only involves a great amount of physiological labour in comminuting the food, and a great expenditure of power and time in dissolving and absorbing it, but throws a great amount of wholly profitless labour upon those excretory organs which have to get rid of the nitrogenous matter, three-fourths of which, as we have seen, is superfluous.'

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[1] *Elements of Physiology* (Macmillan & Co.), 1866, p. 142.

Hence, to avoid such an evil, experience teaches us to mix fats or amyloids with albuminous foods, and these, supplemented by the salts found in the body and furnished by vegetable and other matters, make up the total necessary foods for sustaining life.

It is impossible here to discuss the relative value of foods, or the politico-economical aspects of the question, or the various influences exerted by age, time, climate, and other conditions upon the quantity or quality of foods required. These questions have been ably treated in separate treatises by Letheby, Smith, Hassall, and others, to which, excellent as they are, we must refer our readers.

We, however, quote on the next page a table from Letheby's work[1] 'On Food,' showing the nutritive values of food. It should be stated that in the construction of this table Letheby has calculated the carbonaceous matters as starch, for the reason that the fattening and respiratory values of starch, gum, fat, &c., are very different, as already explained. The power of fat is about 2·5 times that of sugar.

To enter at all into the life history of tissues,—to attempt to depict the actual manner in which the living

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[1] *On Food*, by Dr. H. Letheby, p. 5. Baillière, Tindall & Cox, 1872.

NUTRITIVE VALUES OF FOOD.

Article	Water	Albumin, &c	Starch, &c	Sugar	Fat	Salts	Total per cent.		Carbonaceous to one Nitrogenous	Total per cent.	
							Nitrogenous	Carbonaceous calculated as Starch.		Nitrogen	Available Carbon
Bread . . .	37	8·1	47·4	3·6	1·6	2·3	8·1	55·00	6.8	1·25	28·21
Wheat flour . .	15	10·8	66·3	4·2	2·0	1·7	10·8	75·50	7·0	1·66	38·57
Barley meal . .	15	6·3	69·4	4·9	2·4	2·0	6·3	80·30	12·8	0·97	36·61
Oatmeal . . .	15	12·6	58·4	5·4	5·6	3·0	12·6	77·80	6·2	1·94	40·44
Rye meal . . .	15	8·0	69·5	3·7	2·0	1·8	8·0	78·20	9·8	1·23	38·48
Indian meal . .	14	11·1	64·7	0·4	8·1	1·7	11·1	85·35	7·7	1·71	43·09
Rice . . .	13	6·3	79·1	0·4	0·7	0·5	6·3	81·25	12·9	0·97	39·03
Peas . . .	15	23·0	55·4	2·0	2·1	2·5	23·0	62·65	2·7	3·54	38·55
Arrowroot . .	18	—	82·0	—	—	—	—	82·00	—	—	36·44
Potatoes . . .	75	2·1	18·8	3·2	0·2	0·7	2·1	22·50	10·7	0·31	10·98
Carrots . . .	83	1·3	8·4	6·1	0·2	1·0	1·3	15·00	11·5	0·20	7·28
Parsnips . . .	82	1·1	9·6	5·8	0·5	1·0	1·1	16·65	15·1	0·17	7·91
Turnips . . .	91	1·2	5·1	2·1	—	0·6	1·2	7·20	6·0	0·19	3·76
Sugar . . .	5	—	—	95·0	—	—	—	95·00	—	—	42·22
Treacle . . .	23	—	—	77·0	—	—	—	77·00	—	—	34·22
New Milk . .	86	4·1	—	5·2	3·9	0·8	4·1	14·95	3·6	0·63	8·55
Cream . . .	66	2·7	—	2·8	26·7	1·8	2·7	69·55	25·7	0·42	32·17
Skim milk . .	88	4·0	—	5·4	1·8	0·8	4·0	9·90	2·5	0·68	6·26
Butter milk . .	88	4·1	—	6·4	0·7	0·8	4·1	8·15	2·0	0·63	5·53

Cheddar cheese	36	28·4	—	—	31·1	4·5	28·4	77·75	2·7	4·37	47·77
Skim cheese	44	44·8	—	—	6·3	4·9	44·8	15·75	0·3	6·90	27·82
Lean beef	72	19·3	—	—	3·6	5·1	19·3	9·00	0·5	2·97	12·98
Fat beef	51	14·8	—	—	29·8	4·4	14·8	74·50	5·0	2·28	39·99
Lean mutton	72	18·3	—	—	4·9	4·8	18·3	12·25	0·7	2·82	13·95
Fat mutton	53	12·4	—	—	31·1	3·5	12·4	77·75	6·3	1·91	40·33
Veal	63	16·5	—	—	15·8	4·7	16·5	39·50	2·4	2·54	25·22
Fat pork	39	9·8	—	—	48·9	2·3	9·8	122·25	12·5	1·51	58·89
Green bacon	24	7·1	—	—	56·8	2·1	7·1	167·00	23·5	1·09	77·52
Dried bacon	15	8·8	—	—	73·3	2·9	8·8	183·25	20·8	1·36	85·53
Ox liver	74	18·9	—	—	4·1	3·0	18·9	10·25	0·6	2·91	13·34
Tripe	68	13·2	—	—	16·4	2·4	13·2	41·00	3·1	2·04	24·36
Poultry	74	21·0	—	—	3·8	1·2	21·0	9·50	0·4	3·23	13·99
White fish	78	18·1	—	—	2·9	1·0	18·1	7·25	0·4	2·79	11·64
Eels	75	19·9	—	—	13·8	1·3	9·9	34·50	3·5	1·53	19·93
Salmon	77	16·1	—	—	5·5	1·4	16·1	13·75	0·8	2·48	13·60
Entire egg	74	14·0	—	—	10·5	1·5	14·0	26·25	1·9	2·16	18·18
White of egg	78	20·4	—	—	—	1·6	20·4	—	—	3·14	9·49
Yolk of egg	52	16·0	—	—	30·7	1·3	16·0	76·75	4·8	2·46	41·55
Butter and fats	15	—	—	—	83·0	2·0	—	207·50	—	—	92·22
Beer and porter	91	0·1	—	8·7	—	0·2	0·1	8·70	87·0	0·2	3·92

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[1] The available carbon comprises all the carbon of the carbonaceous constituents of the food, and the carbon of the nitrogenous parts, after deducting the carbon of the urea which is excreted; 100 of dry nitrogenous matter yielding 31·23 urea.

organs and tissues assimilate from the food, the matter they require to keep them perfect and in good working order, would be to enter the domain of pure physiology. To a large extent, work of this kind is not within the powers of observation; but we may refer our readers to such works as that of Lionel Beale upon 'Bioplasm'[1] for a description of what is known upon the subject. Bioplasm is a living, moving, and growing matter which exists in every part of the body, and it has the power of taking up lifeless material, which it changes in such a way that its elements are assimilated and become living matter. After a time the living matter undergoes further change. It, or a part of it, is resolved into non-living substances, which may be gaseous, liquid, or solid. Bioplasm in fact, occurring in every tissue, in every part of the living body, is germinal matter possessed of a power of selection of elements from the pabulum supplied to it, by which it converts dead or lifeless matter into living matter. But all bioplasm must die, and by the death—or in other words, by the specific changes which result at certain stages—tissue results, and hair, skin, bone, nerve, and muscle are produced.

Whether the oxygen taken in respiration is the cause of decomposition of the tissues or not is difficult to decide. Carl Voit[2] insists that it is a consequence of the tissue decomposition; the tissues splitting up independently of oxygen, and forming products which combine with the oxygen which is inspired. Voit further divides the albumin of the body into circulating albumin (that contained in lymph) and organ albumin. He supposes that the first of these readily undergoes decomposition, whereas organ albumin is not subjected to the conditions of decomposition until it has become converted into circulating albumin.

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[1] *Bioplasm, &c.* By Lionel S. Beale, M.B., F.R.S. J. & A. Churchill. 1872.

[2] *Zeitschrift für Biologie*, viii. 297–388.

F. Hoppe-Seyler[1] contests these opinions of Voit, and maintains that the consumption of albuminous matters in the organism takes place in the living cells of the tissues and not in the lymph in which they are bathed as held by Voit, or in the blood as was maintained by Lehmann, Frerichs, Bidder, and Schmidt. Such consumption, he contends, may be effected by oxidation or through the agency of ferments. When oxidation is the cause, Hoppe-Seyler believes it to be due to the direct action of ozone produced in the tissues from oxygen. This latter doctrine is eminently improbable, and, indeed, there is so much speculation in all these matters, as scarcely to repay the student for following them. Those who may desire to learn further of such matters may consult the publications referred to, as also one by E. Pflüger on 'Physiological Combustion in Living Organisms,'[2] and the writings of E. Becquerel[3] upon the operation of electrocapillary forces in the phenomena of nutrition. After all it may be fairly said without prejudice that, regarding these deep questions concerning vitality and its sustenance, our knowledge is neither sufficiently comprehensive or precise to admit of final statements.

The organs through which the excretory matters of the body are eliminated, do not form the various substances thus got rid of. But it is otherwise with glands which furnish substances destined to play a further *rôle* in the economy. These seem to effect a special transformation of specific matters presented in the blood or elsewhere, sugar of milk, for example, being produced in the mammary gland in this way, but the true mechanism of such processes is entirely without explanation. Generally, these processes are referred to the action of ferments, but no satisfactory explanation has been afforded of the fact that from a similar matter totally different substances should be produced by different causes or agents.

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[1] Pflüger's *Archiv.* vii. 399-428.

[2] *Ibid.* x. 251–368.

[3] *Compt. Rend.* lxxx. 411–417.

CHAPTER XI.

RESPIRATION—BREATH—MUSCLE OXIDATION.

WE have seen that the blood conveys to the body the food which has been previously prepared by the various digestive and alterative processes antecedent to the time when it enters the blood. The composition of the blood may therefore vary to some extent according to the nature of the food eaten and other causes. By the action of the heart the blood is pumped through the lungs (into the pulmonary arteries) at the rate of 22 to 27 lbs.[1] in one minute, and here it undergoes a process of oxidation which we must now consider more in detail. We have already described the colouring matter of the blood, but it is now necessary to review a few of its spectroscopic characters. A sufficiently diluted solution of hæmatocrystalline, when examined spectroscopically, exhibits two bands of absorption: the blood of all vertebrates when viewed within the living blood-vessels shows also the same bands, therefore there can be no doubt that the colouring matter is not radically changed by the process of extraction. Now Stokes many years ago demonstrated that these two bands were characteristic of arterial blood; venous blood exhibiting but one band; and that these properties are in direct connection with the colouring principle of the blood there is no doubt, because a solution of hæmato-crystalline can be deprived of its oxygen, and it then gives the single absorption band of venous blood; by shaking it again with oxygen the second band is restored.

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[1] Other determinations do not agree with this figure, 10 lbs. being the amount estimated.

Now all researches, even including those most recently published, show that the oxygen which is absorbed into the blood during respiration, is not held merely in solution in a dissolved state, but at least a part of it exists in combination with this hæmato-crystalline. For instance, Bert,[1] who has devoted much time to the determination of the quantity of oxygen which can be absorbed by the blood under various atmospheric pressures, and also Fernet, who has conducted similar investigations, both conclude that a part of the oxygen in the blood is independent of barometric pressure, and consequently it exists in a state of combination with the colouring matter. This combined oxygen is unaffected in amount by barometric pressure; it is only the lesser quantity of dissolved oxygen which can be so influenced. From all this, it appears certain that the corpuscles of the blood are the carriers of oxygen, which, entering into combination with the hæmato-crystalline, is carried by the blood-circulation to the most distant and hidden parts of the body, where at all points it is given up to the body; the tissues in their turn give up carbonic acid, water, urea, and other excrementitious products of the blood. The carbonic acid is absorbed by the blood, and is contained therein partly in the state in which it exists as in soda water, but partly also in combination with alkaline bases, particularly sodium. In the lungs, oxygen is absorbed on the one hand, and carbonic acid is given out and respired; it is easy enough to understand how the free carbonic acid is liberated, but not so simple to explain the liberation of that part previously in combination with alkaline bases. Thudichum supposes that when the venous blood reaches the small breathing cells, the hæmato-crystalline is partly oxidised into what he calls hematic acid, and this passing into the serum at the same moment, decomposes the carbonates in the blood, setting free carbonic acid which with the watery vapour escapes through the lung tissue into the respiratory passages. It is true that Liebig disputed the presence of carbonates in the blood, but it has been since shown that the method of analysis upon which he based his opinion was such as to prevent their discovery. Confirmative of the process of blood oxidation which has been described, is the prediction of John Stuart Mill, made in 1856,[1] and which resulted from a logical consideration of Graham's researches upon diffusion. This work of Graham brought out the fact 'that gases have a strong tendency to permeate animal membranes, and diffuse themselves through the spaces which such membranes enclose, notwithstanding the presence of other gases in those spaces.' Mill then says: 'The exchange of oxygen and carbonic acid in the lungs is not prevented, but rather promoted by the intervention of the membranes of the lungs and the coats of the blood-vessels between the blood and the air. It is necessary, however, that there should be a substance in the blood with which the oxygen of the air may immediately combine; otherwise, instead of passing into the blood it would permeate the whole organism; and it is necessary that the carbonic acid, as it is formed in the capillaries, should also find a substance in the blood with which it can combine, otherwise it would leave the body at all points, instead of being discharged through the lungs.'

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[1] *Compt. Rend.* lxxx. 733–736.

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[1] *System of Logic*, 4th Edit., 1856, vol. i. p. 523.

Thus it is seen that the necessities of reasoning are entirely satisfied and fulfilled by the theory of the process of blood oxidation held to-day; but chemists have not yet succeeded in isolating the body which they know exists, viz., the particular combination of the colouring matter present in blood corpuscles with oxygen, or hematic acid as Thudichum terms it.

P. Schützenberger, in his work on Fermentation,[1] has described a beautiful experiment illustrative of the oxidising power of blood. He causes red arterial blood to circulate through a sufficiently long system of hollow tubes constructed of goldbeater's skin and immersed in a mixture of yeast diffused in fresh serum without globules, at a temperature of 35° C. (95° F.). Under these conditions the blood gives up its oxygen to the yeast through the walls of the tubes, and then passes out black and venous at the other extremity.

Schützenberger, in conjunction with Ch. Risler,[2] has determined the amount of oxygen contained in blood by adding to a given quantity an excess of standardised sodium sulphite, and estimation of the excess in an atmosphere of hydrogen. The quantity of oxygen may be thus determined within 2 per cent. The authors show that the oxygen of the blood does not act on the sulphite like free oxygen, but like oxygen combined with ammoniacal cupric oxide. Fresh ox blood, saturated with oxygen, shows in respect of the sulphite an oxidising power equal to 45 per cent. of oxygen, whereas where it is deoxidised by the air-pump, or by carbonic oxide, this becomes reduced to 25 or 26 per cent. The oxygen removable therefore from blood by the air-pump is about 19 per cent.[1]

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[1] English Edition, 1876 (King & Co.).

[2] *Compt. Rend.* lxxvi. 440–442.

We have already considered the process by which blood becomes oxidised in the lungs; the study of the mechanism belongs to the science of pure physiology. It is sufficient therefore to state the main points.

The pulmonary capillaries are wide and thin-walled, and are arranged so that they form a complete network with but small meshes. The blood in the capillaries is separated from the air only by their own walls and the delicate thin lung membrane. These conditions favour the processes of diffusion which, so far as they have a bearing upon respiration, may be thus stated. Gas which is held mechanically by any solution has a tendency to diffuse into any atmosphere to which it may be exposed until it is present in that atmosphere in a proportion corresponding to that remaining in solution. Hence this law applies to the carbonic acid dissolved in venous blood. Again, gases separated from each other by a porous partition diffuse into each other with a rapidity inversely proportional to the square roots of their densities. This law applies to the carbonic acid set free in the capillaries by the action of so-called hematic acid upon the sodic carbonate of the blood ; it also applies to the oxygen in the air on the other side of the lung membrane. By the application of these principles we obtain at least a general sort of appreciation of the *modus operandi* in the lung tissue.

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[1] Serum dissolves about as much oxygen as water at 100° F., viz. $\frac{1}{40}$ of its bulk, therefore each pound of blood would dissolve about 12 cc. of oxygen ; and it has been calculated that three times this quantity really enters the blood.

The expired air is saturated with aqueous vapour, and registers a temperature about that of the blood, varying between 35° and 36° C. Ten thousand parts of ordinary air contain 2,100 parts of oxygen, 7,900 of nitrogen, and 3 of carbonic anhydride; 10,000 parts of expired air contain from 1,500 to 1,600 parts of oxygen, 7,900 of nitrogen, and 470 of carbonic acid.[1] That is to say, the nitrogen is not affected, but on the other hand the air loses 5 per cent. oxygen, and gains an almost equal amount of carbonic anhydride. Vierdot gives 4·7 per cent. of oxygen as removed from the air and 4·3 per cent. of carbonic acid returned to it.

According to Regnault and Reiset,[2] warm-blooded animals both take in and respire a trace of nitrogen, but it undergoes no chemical change, and is partly exhaled by the skin. Pettenkofer has also found traces of hydrogen, marsh gas, and ammonia to be present in expired air; these probably arise from the digestive processes, and may at times amount to more than traces. We cannot here refer at all in detail to the many various researches on respiration which have been carried out of late years, as all of them have a more direct meaning to physiologists than to chemists. Beyond Regnault and Reiset's observations already referred to, Scharling[3] has experimented upon respiration; also Andral and Gavarret,[4] Pettenkofer and Voit,[1] Dr. Edward Smith,[2] E. Pflüger,[3] and Moritz Nussbaum[4] and others.

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[1] Huxley, *Elements of Physiology*, p. 85.

[2] *Ann. de Chimie*, III. xxvi. 511.

[3] *Liebig's Annal.* xlv. 214, and lvii. 1.

[4] *Ann. de Chimie*, III. viii. 129.

The sort of apparatus employed in the study of the respiratory process consists of an air-tight chest large enough to hold the animal operated upon, and capable of being fed with air by means of a pump. Attached to the apparatus are series of vessels, some containing sulphuric acid intended to absorb the water contained in expired air, and others holding caustic potash to absorb the carbonic anhydride exhaled. Dr. Smith, however, used a different apparatus. In this case the air for inspiration was conducted by a caoutchouc tube from a small spirometer by which it was measured, to a mask closely covering the nose and chin. The expired air was passed through another tube (by means of a proper disposal of valves) into the analytical apparatus. The quantity of air passed through the lungs in twenty-four hours is very variable, and depends upon individual habits and bodily conditions. It has been variously estimated. Dr. E. Smith gives from 804,780 cubic inches to 1,568,390 cubic inches. Huxley states[5] that, taking no exercise, it is estimated at 350 to 400 cubic feet, a figure widely different to Dr. Smith's.

The water given off in twenty-four hours is estimated by Smith at an average of 311 grms., and the carbon as carbonic anhydride, as from 7·144 oz. to 11·7 oz.

Dumas has estimated the carbon passing off through the lungs and skin in twenty-four hours at 8½ oz., and

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[1] *Liebig's Annal. Suppl.* Bd. ii. 1.

[2] *Phil. Trans.* 1859, 681.

[3] Pflüger's *Archiv. f. Physiologie*, x. 251–368.

[4] Pflüger's *Archiv.* vii. p. 296.

[5] *Elements of Physiology*, p. 86.

Scharling, as well as Andral and Gavarret, have given similar determinations. Liebig gave a much higher figure, but he only arrived at it from calculations not based upon experiment. Dr. Smith has also ascertained that the oxidation of carbon, so to speak, is most active between the ages of 35 and 40, and less in youth and old age: females exhale somewhat less carbonic anhydride than males, and this is decreased during menstruation; during pregnancy there is an increase. In certain skin diseases the quantity is increased; it is also increased by cold, but diminished by heat. Muscular exertion appears to be the great incitive to active respiration, by which means the amount of carbonic anhydride expired is doubled or even trebled in amount. Asphyxia results whenever the carbonic acid in tidal air reaches 10 per cent.; uneasiness and headache, however, are caused when less than 1 per cent. of the atmospheric oxygen is replaced by other matters. The poisoning, as it is called, of carbonic acid results rather from an interference with the proper function carried out by oxygen in the blood than from any direct action possessed by itself. Every man should have at least 800 cubic feet of air space to himself, and this should be in direct communication with the atmosphere, so that it may be constantly supplied with fresh air as the initial quantity becomes vitiated.

Calculating on the basis that 8·5 oz. of carbon are expired as carbonic acid in every twenty-four hours, and further assuming that 10 lbs. of blood pass through the lungs every minute, then every pound of blood must emit two cubic inches of carbonic anhydride. Again, if 15 per cent. of the oxygen absorbed be allowed for that quantity fixed by hydrogen, then 26·7 oz., or more than 1½ lbs. of oxygen, are consumed daily by every adult.

Barral has published some elaborate researches[1] upon the average assimilation and consumption of food compared with the excreta of the body, but we cannot do more here than quote a table which he has constructed upon his results, notwithstanding that these latter are not free from objection.

QUANTITIES IN OZ. AVOIRDUPOIS OF FOOD AND EXCRETA IN TWENTY-FOUR HOURS.

Period of Year	Consumed			Evolved				
	Food taken		Oxygen absorbed	Water by Skin and Lungs	Carbonic Anhydride	Total Excreta		
						Urine	Fæces	Nasal Secretion
	Solid, not dried	Liquid					Not dry	
July . .	24·4	59 7	27·42	40·27	31·34	36·14	2·66	1·19
December .	39·2	57·9	37·44	45·43	43·32	39·97	5·00	1·15
Or in 100 parts								
July . .	75·4		24·6	36·1	28·8	34·7		0·4
December .	72·2		27·8	33·8	32·3	33·2		0·7
	100			100				

In reference to this table and to the process of respiration generally, it should be stated that the whole of the oxygen inhaled does not return as carbonic anhydride and water; a portion is combined with the matters in the blood, and these products of oxidation, particularly urea, leave the body in the urine.

Now that an apparatus has been invented in which persons may live for days together and be observed, and all the products of respiration and the excreta be determined and analysed, it is possible to obtain a more exact knowledge of the history of oxygen within the body.

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[1] *Annales de Chimie*, III. xxv. 129.

Already it has been found that during sleep a quantity of oxygen is stored up in the body, particularly in the muscles, and this is ready for the production of force when required. The means whereby oxygen is thus stored up are not known exactly, but the myochrome or colouring matter of the red muscles appears to be identical with the hæmato-crystalline of the blood, and hence it is probable that it is with this principle that the oxygen stored up in the muscles is in combination.

Paul Bert has studied the poisonous nature of oxygen or compressed air upon animals, and in a recent paper[1] he confirms and extends these observations. In dogs, convulsions begin when the external pressure of oxygen is about 3½ atmospheres, or 17 atmospheres of air, and death occurs at 5 atmospheres of oxygen. He examined the blood and found that oxygen acts as a rapid poison when arterial blood contains 35 per cent., or nearly double the normal amount. These convulsions and death are due to an exaggeration of the excito-motor power of the spinal cord, and are accompanied by a considerable and constant diminution in the internal temperature of the animal: that is to say, oxidation is hindered.

Far more unreasonable, however, is the conclusion of A. Fränkel[2] to the effect that a diminished supply of oxygen is invariably followed by an increase of urea in the urine of animals, and therefore an increase of albumin degradation; he supports his conclusion by the gratuitous assumption that albumin degradation and urea formation bear no absolute relation to the amount of oxidation going on in the organism, oxygen being further assumed by him to act only upon dead and not living nitrogenous matters! As the act of life is intimate with the act of oxidation, and considering that urea is derived from the oxidation of albumin, it is not easy to fall in with such a conclusion, more especially if we keep in mind Frankland's experiments on muscular force.

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[1] *Compt. Rend.* lxxvi. 443–446.

[2] *Chem. Centr.* 1875, 708–709.

E. Pflüger has also written much upon the theory of respiration; here it is proposed to refer briefly to two of his more recent ones.

One of these is entitled 'On Physiological Combustion in Living Organisms,' and has been already referred to:[1] it is for the most part of a theoretical nature, and in support of doctrines previously expressed in other earlier papers. Thus the author insists that the living cell regulates the amount of oxygen consumed, and that animal combustion of the cell presupposes not only no active, and only neutral oxygen, but is within wide limits entirely independent of the partial pressure of the neutral oxygen. That is to say, Regnault and Reiset's law that animals absorb the same quantity of oxygen, and eliminate an almost equal amount of carbonic acid, holds good without regard to the pressure of the oxygen that is inhaled. It is not worth while to follow the author through the reasons that he arrays against the supposed and stated presence of ozone in the blood; it is enough to state that its presence has never been established, although Dr. Binz,[2] and others have laboured hard to make the contrary doctrine acceptable.

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[1] Pflüger's *Archiv. für Physiologie*, x. 251–368.

[2] *Chem. Centr.* 1873, 73–75.

In a later paper by E. Pflüger,[1] experiments are described to show that although pure oxygen be respired, the intensity of internal combustion is the same as when air is respired, and Dittmar Finkler and E. Oertmann[2] have confirmed the view that the respiratory mechanism has no influence on the amount of total tissue-metamorphosis.

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[1] Pflüger's *Archiv.* xiv. 1–38.

[2] *Ibid.* xiv. 38–72.

CHAPTER XII.

ANIMAL HEAT—VITAL FORCE—MUSCULAR ACTION.

NOTWITHSTANDING that the breath leaves the body at the temperature of the blood, and that the body itself radiates heat just as other natural objects do, yet animal heat is almost a constant, and is maintained at from 36·6° to 37·7° C. (98° to 100° F.) almost uniformly, while health lasts. This constant temperature is primarily maintained by virtue of the conditions which obtain in the body, and which are essential to life, viz. the generation and distribution of heat within the body. At all points of the body the tissue is undergoing oxidation—metamorphosis—change; it is absorbing oxygen carried by the blood, and breaking up into simpler products; every such act of oxidation is necessarily attended with the evolution of heat. In most chemical reactions there is either an absorption or evolution of heat, and the oxidation of albuminous matters is always accompanied by heat. The supply of oxidisable matter is kept up by the regeneration of the tissues and organs from the nutriment submitted at the same time in the blood. Even apart from tissue change, heat may be produced, for example, by acts of oxidation occurring in the blood itself, such as the burning up of fat or alcohol, or carbohydrates, into carbonic anhydride and water.

In order to diminish the quantity of heat which would have otherwise to be generated in the body itself, animals are provided with natural coverings to their bodies, composed of feathers, wool, or hair, and these prevent the loss of heat by radiation which would otherwise occur. Man, on the other hand, provides himself with clothes to effect the same purpose.

Despretz has shown by experiment that the combustion of one ounce of pure carbon evolves sufficient heat to raise the temperature of 14,200 times its weight of water through 1° F., or enough to convert into vapour 12·63 times its weight of water at the temperature of the blood. The combustion therefore of 8·5 oz. of carbon in the body daily should suffice to evaporate 107·7 oz. of water, or nearly 6·75 lbs., whereas on an average not more than 2·5 lbs. are evaporated daily from the body, calculating on that expired with the breath and that given off by the skin (1·5 lbs.). It is the surplus heat which must be held accountable for the maintenance of the body at a constant temperature, and for the supply of muscular force.

The process of oxidation takes place at every point in the body where vital activity reigns, and the amount of heat liberated is simply proportional to the activity of the chemical changes going on. As this activity is not always of the same extent at all times in all parts of the body; and as some parts of the body are more directly subject to radiation than others, the temperature of the body would be unequal in different parts were it not for the circulation of the blood, which distributes and regulates the heat. It is admitted on all hands that muscular power is derived from that same oxidation which gives rise to and maintains animal heat; but it is an open question whether the oxidisable matter must first become muscle or not, before its oxidation can give rise to muscular force. Liebig maintained that the non-nitrogenous part of food was simply useful as of a heat-producing character; and this doctrine received the support of Ranke, Playfair, and others. On the other hand, with much show of reason, J. R. Mayer maintained that 'a muscle is only an apparatus by means of which the transformation of force is effected, but it is not the material by the change of which the mechanical work is produced.' The blood was regarded by him as a slowly burning liquid, 'the oil in the flame of life.' This doctrine was put forward by Mayer in 1845.

In 1854 Dr. T. Gordon Hake communicated to the 'American Journal of the Medical Sciences' (October), a paper on Vital Force, which he reprinted[1] after Frankland had in 1866 made his well-known experiments on muscular force. In this paper Dr. Hake laid down the principle (previously originated by Mayer), 'that the oxidation of carbon and hydrogen in the lesser circulation was the source of muscular in common with all other vital force.' He 'insisted particularly on the view that a cerebro-spinal system does not generate its own force, but derives it through the chemical changes in the lungs.' Again, he writes: 'In every system the force destined to control organic functions undergoes a metamorphosis; chemical in the lungs, it becomes electrical in the blood-cells, nervous in the cerebro-spinal axis and the ganglia of the sympathetic, endo-muscular in the muscles, and calorific when, as nervous or muscular, its vital act is completed.' It is not possible in this place to follow Dr. Hake through all his potent reasoning; here and there is room and perhaps occasion for a difference of opinions, but in the main his conclusions are beyond refutation. By thus giving attention to his pamphlet based upon experimental data and facts, it is hoped to direct a more extended attention to his views on such an important subject. In support of his theory, which we shall follow somewhat more closely hereafter, cholera may be instanced. In this disease the body temperature sinks as low as 67° F., although the carbon and hydrogen in the blood is oxidised in the usual manner and the products evolved. It is a disease similar in its revealed state to shocks following upon nervous lesions, in which also the body temperature is depressed. Dr. Hake writes, 'We have only to weigh the phosphates ejected daily from the system to adopt the conclusion that the nervous centres do not yield the physical resources through which their own currents are supplied;' and he rejects as a whole the doctrine of a temperature derivable from a mechanical diffusion of heat generated in the lungs.

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[1] *On Vital Force: its Pulmonic Origin, and the General Laws of its Metamorphoses.* By Thomas Gordon Hake, M.D., F.C.S. H. Renshaw, London, 1867.

He believes that the chemical changes as they occur in the blood system and comprised in the act of oxidation, do not result in the evolution of heat, but force, which becomes electric by the agency of the blood corpuscles; and it is certain that this is perfectly consistent with what we know of cell life. On this hypothesis, the blood cells form chains and conductors for the electric current thus generated, and this is subsequently metamorphosed into heat at every point of the system. On reaching the cerebro-spinal centres it becomes vital force—another name for electric force—and this becomes eventually heat, namely, when it is transmitted to enable the consummation of a vital act, such as sensation, muscular motion, or secretion. Faraday and Du Bois Reymond, and hosts of other experimental enquirers, have insisted on the identity of electrical and vital force, and the experiments of Du Bois Reymond in particular go to prove that nerve force is only electric force manifested through media not met with out of living bodies. Of course on Hake's hypothesis, nerve force is derived from the common centre (the brain), where it is stored in the grey matter of which brain matter is partly composed, and from which the nerve tubes spread everywhere. Our author even goes further, and with consummate skill, reasons that when this cerebro-vital force is united in action within the same organic medium with other forces influencing us from without, viz. light, sound, heat, &c., new results are attained, and phenomena of sense and intelligence are observed. In anæmia, a disease in which the corpuscles of the blood are seriously diminished, the brain loses somewhat of its intense vital force, the power of attention is defective, forgetfulness obtains, the faculties are slowly exercised, and why? Because the source of vital force, viz. blood oxidation, is interfered with.

The nature and sources of the mind must be considered with Dr. Hake as the grandest problem in science. It is from sharing this impression, and entertaining the rational hope that even in this direction, conclusions are within the attainment of future science, that we have given so much attention to Dr. Hake's theory. This has been done the more readily since all recent science tends to show two things, namely, the unity of force and the possible transmutation of its revealed forms. The form in which force is revealed differs according to the media by which and the conditions under which it is revealed.

We must now return to the attempt made by Frankland to ascertain the origin of muscular force; and we may remind our readers that in theory he differs from Hake only in detail; in fact, he leaves the nervous system as an intervening factor in the transformation of animal force out of consideration.

To ascertain the source of the dynamical power of the animal, it appeared necessary to determine the following problems:[1]—

(1) The amount of force which can be generated by the oxidation of a given weight of muscle in the body;

(2) The amount of force actually exerted by the muscles in the body during a given time; and

(3) The quantity of muscle actually oxidised in the body during the same time.

The first of these problems has been solved by Frankland;[2] but before stating his results it should be explained that a unit of force is that amount which is necessary to lift a kilogramme to the height of a metre. Now Joule has supplied the connection between this unit and the amount of heat which it represents, and this may be thus expressed: 423 metre-kilogs. of force are required to raise 1 kilog. of water 1° C. Frankland found that the combustion of 1 grm. of dry muscle in oxygen gave out sufficient heat to raise 2161 kilogs. to a height of one metre; but as muscle never leaves the body in a completely oxidised state, but mainly as urea, and as muscle and albumin would furnish almost exactly 33 per cent. of their weight of urea, the quantity of heat emitted by the oxidation of one grm. of muscle into urea amounts to 1848 mkgs. instead of the total 2161 mkgs. obtained in perfect combustion.

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[1] Miller's *Elements of Chemistry*, Part III., 3rd Edition, 1867.

[2] *Phil. Mag.* 1866.

Fick and Wislicenus[1] have attempted to solve the second and third problems by raising a known weight (their own bodies) up a given height (in climbing a mountain) and determining the quantity of nitrogen excreted by the kidneys during the effort, and comparing it with that thus escaping before and after the exertion. Although objections have been raised to the method employed, and although these have considerable importance, yet as all possible precautions were taken, the results obtained by the Swiss professors have much interest. Without going into the figures they give, it is shown that the work done, required a consumption of 86·3 grms. muscle, whereas the nitrogen found in the urine only amounted to 30·63 grms. muscle (using Frankland's estimate), so that it appears something besides azotised material was expended in maintaining the manifested energy. Curiously enough, less nitrogen was excreted in the urine during the climbing (5½ hours) than escaped through this channel during an equal period of repose before the ascent! It is true that the Swiss professors placed themselves upon a diet free from nitrogen for one day before the ascent, but altogether the results are singularly confirmative of Mayer's and Hake's hypotheses.

[1] *Phil. Mag.* 1866

Professor Frankland not only determined the force values of albumin, but also of fat and farinaceous matters, in kilogrammetres, and obtained these results:—

1	grm.	of	dry albumin	gave	1781	kilogrammetres.
1	„	„	fat beef	„	3841	„
1	„	„	starch	„	1627	„

In relation to this subject it should be remembered that Frankland's estimate is not without objection, and this objection will remain so long as we are ignorant of the precise manner in which albumin or muscle splits up in the living body.

CHAPTER XIII.

THE URINE AND ITS CHEMISTRY.

The blood which supplies the kidneys is conveyed by the renal arteries from the aorta, and although it is pure so far as carbonaceous waste matters are concerned, it is loaded with the nitrogenous educts of the living body, notable among the constituents being urea and uric acid. The function or act of secretion of the kidneys consists in the removal of these impurities, and this is effected in a sort of dialytic manner. That is to say, as the impure blood filters through the kidneys, the crystallisable and soluble impurities are abstracted from the blood just as a solution of albumin may be freed from salts by dialysis through parchment paper. The secretion is conveyed by the ureters to the bladder, from which it is ejected at will at requisite periods. Although the passing of urine is intermittent, the secretion is really constant, the fluid flowing drop by drop from the ureters into the bladder.

The blood which is thus purified by the kidneys is the purest in the body, but what is remarkable is the absence of fibrin in the plasma of the blood of the renal vein, in which respect it much resembles serum.

General Characters of Urine:—Urine is an amber-yellow coloured fluid, of peculiar odour, and of slightly acid reaction. It may become more acid on standing, owing to certain fermentative processes which set in, and which result in the production of lactic and other acids. Later on, the urea decomposes and ammonium carbonate is produced, and in this way the reaction of the urine becomes, or may become, alkaline.

It should be remarked that urine possesses no inherent tendency to change when kept after evacuation. The changes which do occur, owe at least their initiation to the germs contained in the air; these fall into the urine and set up processes of putrefaction or fermentation in the way described in a special place (see Chapter XXII.). Urine is not always acid when passed, but frequently neutral or even alkaline.

The cloud which forms in urine on standing, consists of mucus and the epithelium of the urinary passages, but other deposits and changes are liable to occur, and these generally indicate diseased processes at work in the body. More attention will be devoted to this part of the subject hereafter.

The colour of urine, as likewise many of its other qualities, differs according to many circumstances, including the nature of the food, the state of the body immediately preceding micturition, the general state of the health, and so on.

As certain articles of food influence the colour of urine, so certain other substances influence its odour. Thus coffee, onions, port wine, garlic, asparagus, and oil of turpentine, each communicates a peculiar odour; oil of turpentine in particular, even when breathed in most minute quantities, gives to the urine an odour of violets.

The general characters of urine are comprised within very wide limits, and this is perfectly comprehensible if we bear in mind that this fluid is really 'the lixivium of the blood,' as Boerhaave termed it. It is a sort of mirror which reflects the processes going on in the body; it is a register influenced by every changing condition in life.

In all animals the urine constitutes the outlet for the nitrogen of effete azotised tissues of the body, though the compounds in which it is excreted vary to a large extent with the animal, and are, indeed, somewhat diverse in individual animals.

According to the proportion of nitrogen contained in the food, the urea excreted in the urine of man increases, an observation originally due to C. G. Lehmann, and one which has been since often confirmed. By restricting himself to an animal diet for twelve days, he excreted daily 53·2 grms. of urea, and 1·4 grms. of uric acid, while upon a purely vegetable diet, extending over an equal period, he excreted daily 22·5 grms. urea, and 1 grm. uric acid, and by subjecting himself to a far less nitrogenous diet, the urea excreted sank to 15·4 grms. daily.

It is impossible in the limits of this work to describe these general characters in any great degree of minuteness, and this will not therefore be attempted. We shall study the chemistry of healthy urine pretty broadly, and indicate its main features in pathology. Anything beyond this is as unnecessary as it would be laborious, inasmuch as several excellent treatises on urine already exist, and to these we must refer our readers. The most comprehensive and accurate treatise of this kind is one, the second edition of which Thudichum has recently lished,[1] and which the writer has freely consulted in what follows.

The quantity and ingredients of the urine vary greatly according to the time of day, the condition of the alimentary canal, the nature of the food, and the temperature and hygroscopic condition of the atmosphere. About one half of the water ingested into the body leaves it through the kidneys, the other half escaping by the lungs, the skin, and the fæces.

Huxley states that an average healthy man excretes by the kidneys about 50 oz., or 24,000 grains of water a day, and in this are dissolved about 500 grains of urea, but not more than 10 or 12 grains of uric acid.

From a table constructed by Thudichum it is shown that the urine of twenty-four hours amounts to, on the average, from 743 c.c., to nearly 3,000 c.c., but of course the quantity of fluid may be, under given conditions, very much more or less. Thus taking the mean quantity at 86 c.c. per hour, it may rise as high as 1,000 c.c. (after taking large quantities of mineral water) or as low as 37 c.c. (on a very dry diet). During sleep the secretion of urine is less active, and the mean quantity is 58 c.c. per hour. As regards the amount of effete matter contained in urine in health, it is in direct proportion to the activity or work of the body. Definite propositions regarding the attitude of certain diseases may be made upon the registered quantity and properties of the urine.

The average specific gravity of urine corresponds with that of blood serum, and is about 1020. It varies, however, between 1018 and 1040, and the solid constituents range between 42 and 93 parts per thousand. Thudichum writes, 'in disease generally where little solid food is taken, the amount of solids sinks from the daily 60 to 50 and 40 grammes' per twenty-four hours. But in life the solids of urine never fall below a certain standard, because even where food cannot be taken, the body lives at its own expense, on its own albumin and fat, as hybernating animals do, and, as a consequence, emaciation is produced.

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[1] *Pathology of the Urine.* By J. L. W. Thudichum, M.D. 2nd Edit. J. & A. Churchill, 1877.

Beyond the urea and uric acid contained in urine there are other animal matters and saline principles, amounting to from one-third to the same quantity of the urea present; among these saline matters occur common salt, chloride of potassium, phosphates and sulphates of potassium, sodium, calcium, and magnesium. The urine also contains a small quantity of the same gases as are found in blood, namely, chiefly carbonic acid, a little oxygen, and a trace of nitrogen. In fact, urine may be viewed as blood minus its corpuscles, fibrin, albumin, and colouring matter. The following table is taken by permission from Thudichum's work on the urine already cited.

Average Composition of the Normal Urine of twenty-four hours, of men weighing from 60 to 65 kilos :—

Average quantity from 24 hours	1400 to 1600 cubic centimetres.
Average specific gravity	1·020
Mean amount of solids	55 to 60 grms.
Urea	30 „ 40 „
Uric acid	0·5
Xanthine-like alkaloid	undetermined.
Kreatine	0·3 grms.
Kreatinine	0·45 „
Reducine	undetermined.

Average Composition of the Normal Urine, etc., continued.

Hippuric acid	0·5 grms.
Indigogen	undetermined.
Urrhodinogen	
Phenol-producing substances	
Cresol- " "	
Chromogen of urobiline	
Omichmyl-oxide	
Urochrome	
Acetic acid	0·288 grms.
Formic acid	0·050 grms.
Kryptophanic acid	0·65 "
Carbonic acid	undetermined.
Chlorine	6 to 8 grms.
Chlorides of sodium and potassium	10 " 13 "
Sulphuric acid	1·5 " 2·5 "
Other sulphur compounds containing up to 0·2 grms. of sulphur in 24 hours.	
Phosphoric acid	3·66 grms.
Potassium	undetermined.
Sodium	
Calcium oxide	0·17 grms.
Magnesium oxide	0·19 "
Earthy phosphates	1·28 "
Iron	undetermined.
Ammonia	0·7 grms.
Trimethylamine	undetermined.
Biliary acids	0·012 grms.
Dinitrogenised derivative of sarcolactic acid	undetermined.
Oxaluric acid	
Oxalic acid	

The minor estimates account for 48 out of 55 grms. of solids, the larger estimates for 62 out of 66 grms. of solids.

Urea (CH_4N_2O).

This substance was discovered by Boerhaave before 1720, and was called by him *the essential salt of urine*, but he was in error in regarding it as only a product of putrefaction of urine.

Berzelius obtained the oxalate, and Prout analysed a perfectly pure specimen of urea.

Other chemists found that when decomposed it gives rise to the production of cyanic acid and ammonia, and by evaporation of a solution of these mixed substances Wöhler produced urea artificially. This accomplishment was of extreme importance at that time, because it was then generally thought that urea was one of those substances elaborated by vital processes which could not be produced artificially. Since then, of course, many other animal and vegetable principles have been elaborated in the laboratory, and so-called vital force is now gradually finding its proper interpretation and place.

Urea is a never-failing and principal constituent of urine, and from the fact that it is regularly found present in small quantity in the blood, but not in the juice of flesh, it appears that this substance is produced within the blood; it is only secreted by the kidneys.

It seems certain then, that urea results from the direct splitting up of albumin in the body, and this hypothesis is confirmed by observations which are described in the chapter on albuminous compounds. It will be there seen that Béchamp states to have obtained urea by subjecting albumin to the oxidising influence of potassic permanganate, while Schützenberger seems also to have proved that urea is one of the direct products of the decomposition of all albuminous matters by hydration.

In certain diseases, such as cholera, its excretion is for a time suppressed, and in consequence an increased quantity is found in the blood, in the sweat, and in the cerebro-spinal fluid.

Various observers have detected the presence of urea in other fluids besides blood and urine; thus Wöhler detected its presence in the *liquor amnii.*

The artificial formation of urea may be effected by several processes. Thus by mere evaporation of a mixture of cyanic acid and ammonia urea is produced by the following reaction:—

$$C_2N_2O + 2NH_3 + H_2O = 2CH_4N_2O.$$

The same result is attained when a metallic cyanate and a salt of ammonia are employed in the place of cyanic acid and ammonia. Carbonate of ammonium is resolved to a certain extent into urea by merely heating it in sealed tubes to 150° for some hours, and it is said that ammonic carbamate behaves similarly. The transformation of the first named salt is particularly interesting, as the change virtually consists in a molecular re-arrangement with elimination of the element of water:—

$$(NH_4)_2CO_3 = 2H_2O + CH_4N_2O.$$

Urea may be also obtained by heating a mixture of two parts potassic ferrocyanide with one of peroxide of manganese upon an iron sheet. The mixture ignites and smoulders; this completed, it has to be extracted with water, and the extract mixed with rather more than 20 parts of dry ammonic sulphate. In this way potassic sulphate is formed, and may be removed by crystallisation; the mother liquor contains urea, and this may be isolated by evaporation to dryness and extraction of the dried residue with absolute alcohol.

Urea is also a product of the action of peroxide of lead and other oxidants upon uric acid, while it is likewise produced when alkalies act upon alloxan and kreatine, as well as by the action of sulphuretted hydrogen upon the double fulminate of copper and ammonium. It may be also obtained by the action of phosgene gas ($COCl_2$) upon ammonia and by the reaction which takes place, according to Natanson, between ammonia and carbonic ether ($((C_2H_5)_2CO_3)$) at a temperature of 182°C., thus:—

$$(C_2H_5)_2CO_3 + NH_3 = \overbrace{C_2H_5,H_2N,CO_2}^{\text{Carbamic ether}} + \overbrace{C_2H_5HO}^{\text{Ethylic alcohol}}$$

and

$$C_2H_5,H_2N,CO_2 + NH_3 = \overbrace{CH_4N_2O}^{\text{Carbamide (urea)}} + \overbrace{C_2H_5HO}^{\text{Alcohol}}$$

Several methods are available for the extraction of urea from urine or other animal fluids.

a. Urine is rendered strongly alkaline by means of baryta (5 grms. to the litre), after which a strong solution of nitrate of barium must be added so long as a precipitate is produced. The mixture is then to be filtered, neutralised with nitric acid, and evaporated to dryness, and the residue extracted with absolute alcohol, from which extract the urea may be crystallised after concentration.

b. If the urine or other fluid be albuminous, Thudichum recommends treating it at once or after concentration with alcohol, and subjection of the residue obtained by evaporation of the alcoholic extracts, to the above described baryta-process.

c. The urine is to be concentrated to a thin syrup and then treated with its own volume of nitric acid, keeping the mixture cool. In this way nitrate of urea is formed, and crystallises out. It is purified by recrystallisation from water, and decolorisation with animal charcoal. To get urea perfectly pure, the nitrate must be redissolved in water, neutralised by potash or potassic carbonate, allowed to crystallise, filtered from the nitrate of potassium crystals, the mother liquor evaporated to dryness and extracted with alcohol.

d. The urine is to be concentrated and treated with an excess of strong solution of oxalic acid; this precipitates the urea as oxalate. On redissolving the minute crystals in water, and warming the solution with calcic carbonate, decomposition ensues, calcic oxalate is precipitated, and urea remains in solution, and may be purified by recrystallisation.

General Characters of Urea.—Urea crystallises from water in quadratic prisms with a rectangular terminal plane, and from alcohol with octahedral planes; the crystals polarise with a faint blue colour.

It is a colourless substance with a somewhat bitter saline taste, and is soluble in its own weight of water, dissolves in five parts of alcohol of 0·816 specific gravity at ordinary temperatures, and in its own weight of boiling alcohol. It is insoluble in ether.

It may be decomposed by acids, alkalies, heat, certain salts, and various ferments, such as yeast and those which abound in putrid matters. It is decomposed by nitrous acid as follows:—

$$CH_4N_2O + N_2O_3 = CO_2 + 4N + 2H_2O,$$

and a similar decomposition is effected by nitric acid containing nitrous acid, or by a nitric acid solution of the lower nitrite of mercury.

When fused with potash or treated with concentrated sulphuric acid, urea is resolved into carbonic acid and ammonia. Heat and alkalies decompose it similarly: if baryta be employed as the agent of decomposition, carbonate of barium is of course produced, and Bunsen, by weighing the carbonate thus formed, determined quantitatively the amount of urea operated upon.

Ferments split up urea into the same products as alkalies; that is to say, they act (as shown elsewhere) as hydrating agents:—

$$CH_4N_2O + H_2O = CO_2 + 2NH_3.$$

With alkaline hypochlorites and hypobromites, urea decomposes, yielding most of its nitrogen in the gaseous form, the carbonic anhydride being simultaneously absorbed, and several very useful processes[1] for the quantitative determination of urea have been based upon this fact. The modification employed by Russell and West[2] is perhaps the best. When a solution of urea in admixture with argentic nitrate is subjected to evaporation, nitrate of ammonium is produced, and cyanate of silver forms and may be crystallised out.

$$2(CH_4N_2O) + 2AgNO_3 = 2NH_4NO_3 + AgC_2N_2O_2.$$

Urea melts at 120° C., and at slightly higher temperatures is decomposed, yielding ammonia, cyanate and carbonate of ammonia, and leaving cyanuric acid in the retort. At higher temperatures this cyanuric acid decomposes, leaving a white residue of melanuric acid, thus:—

$$\overbrace{4CH_4N_2O}^{\text{Urea}} = \overbrace{C_3H_4N_4O_2}^{\text{Melanuric acid}} + CO_2 + 4NH_3.$$

By heating urea in sealed tubes to 140° C., in contact with water, it decomposes by a reaction exactly the reverse of that by which its synthesis is effected, thus:—

$$CH_4N_2O + 2H_2O = 2(NH_4)CO_3;$$

that is to say, two molecules of water are assimilated, and ammonic carbonate is produced. This change sometimes takes place in the urine through influences excited by the mucus of the bladder, and the ammoniacal odour of such urine is due to this cause.

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[1] E. W. Davy, *Phil. Mag.*, June 1854, p. 385.

[2] *Journ. Chem. Soc.*, August 1874.

The chemical relations of urea are particularly interesting, and deserve a few words. By the displacement of a certain number of hydrogen atoms, a whole series of compounds, known as compound ureas, may be produced, and their constitution is readily explicable on the assumption that urea itself is carbamide, or the diamide of carboxyl, $CO(NH_2)_2$, or a body in which two hydrogens of the double molecule of ammonia are replaced by the radical CO (carboxyl). Sulpho-carbamide or sulpho-urea has the constitution $CS(NH_2)_2$, and is related to ammonic sulphocyanate just as carbamide is related to ammonic cyanate. It is obtained by heating dry sulphocyanate of ammonium to 170° C. for some hours. To return now to our original proposition regarding compound ureas.

Ammonic cyanate, $CNO(NH_4)$, as already shown, readily becomes converted into the metameric body urea or carbamide, $CO(NH_2)_2$. Cyanic acid also readily combines with the primary and secondary monamines (and diamines), with the evolution of heat and the formation of so-called compound ureas. Thus ethylcarbamide, or ethylurea, is produced by the reaction—

$$CNOH + NH_2C_2H_5 = CO\left\{\begin{matrix} NH.C_2H_5 \\ NH_2, \end{matrix}\right.$$

in which ethylamine and cyanic acid undergo the process of combination. Again, diethylurea is produced by the action of diethylamine upon cyanic acid :—

$$CN.OH + NH(C_2H_5)_2 = CO\left\{\begin{matrix} NH \\ N(C_2H_5)_2. \end{matrix}\right.$$

Compound sulpho-ureas are also obtainable and similarly explicable.

There are many other series of bodies, such as the so-called ureides and urethanes, of much interest to the chemist, but having no particular importance from a physiological point of view. Some of these substances will be studied hereafter.

The Compounds of Urea.—Urea forms three distinct compounds with oxide of mercury, viz. $CH_4N_2O + HgO$; $2CH_4N_2O + 3HgO$; and $CH_4N_2O + 2HgO$.

By mere evaporation with sodic chloride urea gives rise to the double salt $CH_4N_2O + NaCl + H_2O$.

The nitrate CH_4N_2O, HNO_3, and oxalate $2(CH_4N_2O), C_2H_2O_4$, have been already described.

Liebig has described[1] three curious compounds of urea, obtained from it and mercuric nitrate; they are represented by the formulæ:—

$$CH_4N_2O + HgO, HNO_3$$
$$CH_4N_2O + 2HgO, HNO_3$$
$$2(CH_4N_2O) + 3HgO, 2HNO_3.$$

These substances are formed when a solution of urea is treated with one of nitrate of mercury, the determining conditions being the relative proportions of the two substances and the amount of free acid in the mercurial solution. Upon the formation of the second of these compounds Liebig based a method for determining the amount of urea in urine volumetrically. This process with all modifications is fully described in Thudichum's work on the urine and elsewhere, so that it is unnecessary to enter into its consideration here.

Physiological quantity of Urea excreted.—A healthy man discharges from 30 to 40 grms. of urea in 24 hours, but of course the quantity varies within certain limits caused by individual circumstances, such as size, and weight of body; nature and quantity of food. In fact, urea is the expression of tissue change or disintegration, as is shown by the fact that its secretion and discharge goes on even without food. Dr. E. Smith found as the result of observations upon himself, that the average hourly excretion of urea, in the 24 hours, amounted to 1·4 grms., while the average at night per hour was 1·07 grms.

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[1] *Ann. Chem.* 85, 294.

It was originally thought that food could not give rise to the production of urea (among other products of change) without first forming part of some vital tissue, but more modern researches tend to show that vitality consists more in the changes occurring in the blood, and that these changes may result in the direct production of urea. (See Chapter on 'Nutrition,' &c.)

Pathological quantities of Urea.—An excess of urea is secreted during certain stages of all acute febrile disorders, such as typhus fever, pneumonia, &c., when the quantity may rise, according to Thudichum, as high as 50 to 80 grms. per 24 hours. So soon as the fever abates the quantity sinks. In other diseases of a chronic nature and accompanied by impaired nutrition, the amount of urea excreted falls below the average, and Thudichum illustrates this by a case of a lady who suffered from tumour and an anæmiated condition of the body, in which only 5 grms. of urea were contained in the 24 hours' urine.

Sometimes the amount excreted becomes less by affections of the kidneys, in which case the amount present in the body becomes unduly large and causes the cachexia known as uræmia.

Uric Acid, $C_5H_4N_4O_3$.

This substance, originally discovered by Scheele before the year 1776, occurs apparently more or less in the urine of all classes of animals. In that of man its amount is not great, while on the other hand it is largely contained in the urine of snakes. Prout found in the dried residue from the urine of boa-constrictors more than 90 per cent. of uric acid, and Simon determined the presence of nearly an equally great percentage in that from rattlesnakes.

Uric acid forms a principal constituent of urinary calculi and deposits, but of this subject we shall treat more fully hereafter. It is only rarely that the acid occurs in urine in such large amount as to spontaneously deposit with red colouring matter attached, on cooling and standing; moreover such deposits consist for the most part not of free uric acid but of urates.

In gout it is found in the blood and other juices, while it enters largely into the constitution of the concretions and deposits which are not unfrequently formed near the joints.

It is best obtained in a pure state from the excrements of serpents by dissolving or extracting them in hot dilute alkaline solutions (potash or soda) and boiling therewith until all urate of ammonium is decomposed. On then precipitating with hydrochloric acid, flakes of uric acid are thrown down, which only require re-dissolving in potash, and re-precipitation with acid, to be comparatively pure. The scales thus obtained consist of small rhombic plates.

By decomposition of a cold saturated solution of potassic urate with hydrochloric acid, larger crystals are obtained with $2H_2O$, which water of crystallisation is expelled at 100° C. In the purification of uric acid, it is necessary to avoid long boiling with strong potash, as otherwise a potassium salt of uroxanic acid ($C_5H_{10}N_4O_6$) is apt to form.

To obtain uric acid from human urine, this should be treated while fresh with about 5 per cent. hydrochloric acid, and the mixture allowed to stand for twenty-four or more hours in a warm place. In this way the urates are decomposed, and yellowish or reddish crystals of the acid are deposited. Or the urates may be obtained by concentration of the urine, and then by decomposition of the removed deposit and purification by the potash process above described, the free acid may be obtained.

When pure, uric acid is a white crystalline powder, almost insoluble (one in 10,000 parts) in cold water, and only slightly soluble in boiling water; insoluble in alcohol and ether, but readily dissolved by strong sulphuric acid, and re-precipitable from this solution by water.

The urates are much more soluble than the free acid. The acid salts of ammonium, sodium, and calcium are frequent ingredients of urinary calculi.

The most readily applied test for uric acid consists in moistening it with dilute nitric acid, whereby alloxanthine ($C_8H_4N_4O_7$) is produced, and this, when gently warmed with ammonia, produces a purple coloration, due to the production of murexide or purpurate of ammonium ($C_8H_4(NH_4)N_5O_6$).

Strecker found that by the reducing action of a weak amalgam of sodium upon uric acid, xanthine ($C_5H_4N_4O_2$)

is obtained in the first place, and subsequently hypoxanthine ($C_5H_4N_4O$), and we shall see hereafter that uric acid is accompanied in the urine by these less oxidised compounds and also by guanine, $C_5H_5N_5O$.

Compounds of Uric Acid.—Uric acid is dibasic, and hence forms neutral and acid salts. It will be sufficient for the purposes of the present work to give the formulæ and chief characters of these. They are all sparingly soluble in water, but more soluble in alkaline solutions, particularly when heated.

The following salts have been prepared and examined :—

Urate of potassium	$K_2C_5H_2N_4O_3$
Acid urate of potassium	$2(KC_5H_3N_4O_3) + H_2O$
Quadriurate „	$KC_5H_3N_4O_3 + C_5H_4N_4O_3$
Urate of sodium	$Na_2C_5H_2N_4O_3 + H_2O$
Acid urate of sodium	$2(NaC_5H_3N_4O_3) + H_2O$
Quadriurate „	$NaC_5H_3N_4O_3 + C_5H_4N_4O_3$
Acid urate of ammonium	$(NH_4)C_5H_3N_4O_3$
Urate of calcium	$CaC_5H_2N_4O_3 + H_2O$
Acid urate of calcium	$CaC_5H_2N_4O_3 + C_5H_4N_4O_3 + 2H_2O$
„ „ barium	$BaC_5H_2N_4O_3 + C_5H_4N_4O_3$
„ „ magnesium	$MgC_5H_2N_4O_3 + C_5H_4N_4O_3 + 6H_2O$.

The urate of lithium is a more soluble salt than any of the others, and thus it is that lithia water is often prescribed to gouty and other persons who are supposed to suffer from an excessive amount of uric acid in the system.

The neutral urates are unstable and are decomposable by carbonic anhydride. The acid urates are far more permanent salts. The urates of the heavy metals are amorphous insoluble compounds, and are comparatively unimportant.

The deposits of urates in urine occur for the most part (according to Scherer and Bence Jones) with persons who eat much meat and drink but little water; they consist chiefly of acid salts of the alkalies, and particularly potassium.

Decompositions of Uric Acid.—By dry distillation, uric acid is resolved without fusion into ammonium carbonate, hydrocyanic acid, cyanuric acid, urea, and other undetermined substances. By fusion with potash, it furnishes ammonia and the cyanide, carbonate and oxalate of potassium.

By the reducing action of sodium amalgam it gives rise to bodies which will be more particularly described presently.

The most interesting products of decomposition are those which are formed under the influences of hydrating and oxidising agents. First, as to the former.

When heated to 160° or 170° in sealed tubes with strong saturated solutions of hydrochloric or hydriodic acids, the following decomposition ensues :—

$$C_5H_4N_4O_3 + 5H_2O = C_2H_5NO_2 + 3CO_2 + 3NH_3.$$

That is to say, it gives glycocine, carbonic anhydride, and ammonia, and from this reaction it would appear to be a cyanuretted derivative of glycocine or amido-acetic acid.

The products which are formed by the action of oxidising agents vary with the activity and intensity of the action, and are many and interesting. They have been examined by Liebig, Wöhler, Schliesser, Strecker, and Baeyer.

Concentrated nitric acid forms alloxan ($C_4H_2N_2O_5$), urea, and nitrous acid, and the two last-named substances then mutually decompose, giving carbonic acid and nitrogen.

Alloxan, which is simultaneously produced with urea by the action of bromine upon uric acid, is a substance which may be variously prepared, and which, on continued oxidation with bromine, gives carbonic anhydride and parabanic acid; thus:—

$$C_4H_2N_2O_4 + O = CO_2 + C_3H_2N_2O_3,$$

and this latter substance, by the assimilation of the elements of two molecules of water, gives rise to the production of urea and oxalic acid:—

$$C_3H_2N_2O_3 + 2H_2O = C_2H_2O_4 + CH_4N_2O.$$

The formation of urea by the oxidation of uric acid has given rise to the hypothesis that the uric acid of urine is only a part of that primarily produced in the system—that part, in fact, which has escaped oxidation into urea, carbonic anhydride, and water.

Alloxan is resolved into urea and mesoxalic acid by the action of boiling baryta water, thus:—

$$C_4H_2N_2O_4 + 2H_2O = CH_4N_2O + C_3H_2O_5.$$

It seems, then, that although urea is derived from uric acid in two stages, yet it represents the whole of the nitrogenous part of the original uric acid molecule, while the non-azotised part gives rise to mesoxalic acid, or a product of its further change.

It is from a consideration of the characters of mesoxalic acid that the various derivatives of uric acid are best understood. They may for the most part be classed under two great headings, viz. monureides and diureides. In other words, mesoxalic acid, $C_3H_2O_5$, oxalic acid, $C_2H_2O_4$, tartronic acid, $C_3H_4O_5$, glyoxalic acid, $C_2H_4O_4$, malonic acid, $C_3H_4O_4$, and glycolic acid, $C_2H_4O_3$, are each capable of combining with one or two molecules of urea, with the elimination of the elements of water.

Thus alloxan may be viewed as a monureide derived from mesoxalic acid as follows :—

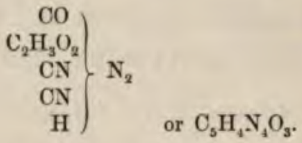
$$C_3H_2O_5 + CH_4N_2O = C_4H_2N_2O_4 + 2H_2O,$$

while uric acid may be classed as a diureide derived from tartronic acid (Gerhardt) as follows :

$$C_3H_4O_5 + 2(CH_4N_2O) = C_5H_4N_4O_3 + 4H_2O.$$

But these considerations are not without their uncertainty, and uric acid has never been obtained in this way.

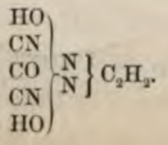
The following formula is given by the author with all reserve, nevertheless it does undoubtedly express some of the decompositions of uric acid in a clearer manner than any other :—



$$\left.\begin{array}{r} CO \\ C_2H_3O_2 \\ CN \\ CN \\ H \end{array}\right\} N_2 \quad \text{or } C_5H_4N_4O_3.$$

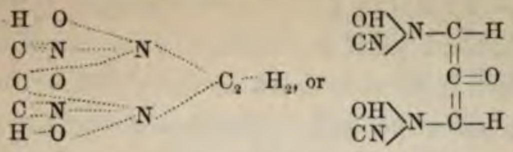
On this speculation uric acid is derived from two molecules of ammonium by the substitution of 2 hydrogen by the CO, the substitution of another hydrogen by the radical ($C_2H_3O_2$) and two others by 2 groups of CN, leaving only one hydrogen not replaced.

The objection to this speculation is that it leaves unexplained the dibasic character of uric acid, which may, however, be rendered intelligible by the following structural formula :—



$$\left.\begin{array}{r} HO \\ CN \\ CO \\ CN \\ HO \end{array}\right\} \left.\begin{array}{c} N \\ N \end{array}\right\} C_2H_2.$$

This is best written as follows :—



which representation exhibits the assumed atomic combinations by the dotted lines.

Without entering further upon this question, it must be admitted that the true constitution of uric acid remains to be determined.

Physiological quantity of Uric Acid excreted.—Thudichum, reviewing the various methods of estimating uric acid in urine, concludes that no process hitherto employed gives the true amount, but that the best method consists in concentration, precipitation by much alcohol, and extraction of the precipitate with water and hydrochloric acid. The residue consists of uric acid which may be purified by warming with caustic potash and reprecipitation by hydrochloric acid during twenty-four hours. In this way he arrived at the result that a healthy man excretes on the average about 0·35 grms. in twenty-four hours.

Pathological processes in which Uric Acid is concerned.—Becquerel determined in various samples of urine the following total quantities of uric acid discharged during twenty-four hours :—

Healthy urine	8.1	grains.
Chlorosis (five cases)	minimum 1·8; max. 6·0	„
Pulmonary emphysema, ext. dyspnœa	4·9	„
Phthisis, tubercles softened	9·1	„
„ three days before death	9·8	„
Morbus cordis, with icterus	9·82	„
Acute hepatitis, with icterus	11·18	„
Icterus	17·75	„
Milk fever	19·0	„

Not only do urates of the alkalies deposit sometimes spontaneously in the urine after emission, but at other times uric acid itself is deposited; in other cases the urate which is thrown down consists almost exclusively of the ammonium salt. The precise conditions upon which these results depend are, to all intents and purposes, unknown. Of course these deposits also occur sometimes in the urinary passages, and Thudichum states that on the average 8·69 per cent. of the cases of calculi present nuclei of urates, while 16·08 per cent. contain layers or crusts of urates. The deposition in the urinary passages appears to occur through two causes, namely, through saturation of the urine with urates and consequent precipitation under given conditions, and (which appears to be the more frequent cause) alkaline fermentation of the urine in the bladder.

Xanthine, $C_5H_4N_4O_2$.

This substance was discovered by Marcet in 1819 as the principal constituent of a rare sort of vesical calculus. It was called by him xanthic oxide, and is known in old publications also as uric oxide and urous acid. Unger discovered its presence in guano. In 1848 Strahl and Lieberkühn established its normal presence in human urine, and in 1858 Thudichum found it as a normal constituent of the human liver in health and disease. Städeler more recently found xanthine diffused through various organs of the body, as the brain, liver, spleen, also muscular tissue, of which it is now considered to be a constant ingredient.

Preparation from Calculi.—The xanthine calculi are dissolved in potash, and from this xanthine may be precipitated in the form of a white powder by means of an acid. Even carbonic anhydride will precipitate it from an alkaline solution.

Preparation from Human Urine.—Precipitate fully with baryta water, filter, and evaporate the filtrate to a syrup; remove the crystals which form on cooling, and boil the mother liquor with solution of cupric acetate. The precipitate thus produced is isolated and dissolved in warm nitric acid, precipitated with nitrate of silver, and the silver salt re-crystallised from dilute nitric acid (about 1 : 10). By suspension in water and decomposition of this silver compound with sulphuretted hydrogen, free xanthine goes into solution, and may be obtained therefrom by concentration and crystallisation.

Thudichum recommends direct precipitation of the urine rendered acid by a mixture of sulphuric and nitric acids with phosphomolybdic acid, and decomposition of the precipitate with baryta water. The solution thus obtained is freed from excess of baryta by means of carbonic anhydride, and the resulting filtrate is fully precipitated with basic acetate of lead and ammonia. On decomposition of the mixed compounds of lead with sulphuretted hydrogen, xanthine goes into solution, and is deposited in yellowish crusts on concentration. It is best purified by preparing from it the argentic nitrate compound, as already described.

It may be similarly prepared from extracts of the liver, brain, and muscular tissue generally. Xanthine also results from the oxidation of guanine with nitric acid containing nitrous acid, and from hypoxanthine by a similar process.

Properties and Characters.—Xanthine forms white amorphous granules or crusts, which, when compressed and rubbed, have a waxy appearance. The caustic alkalies, particularly ammonia, dissolve it freely, but it is not very soluble in water, and is insoluble in alcohol and ether.

A watery solution is precipitated by argentic nitrate, giving a gelatinous mass, which is insoluble in dilute ammonia, but readily soluble in nitric acid. It is also precipitated by mercuric acetate. A hot hydrochloric acid solution, treated with platinic chloride, gives on cooling a yellow double salt of unascertained composition.

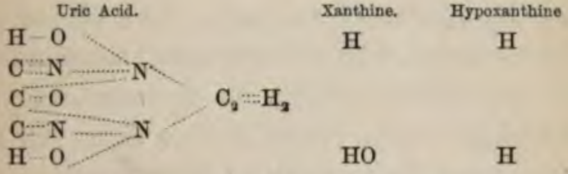
An ammoniacal solution is precipitated by ammoniacal solutions of the chlorides of cadmium and zinc; these white precipitates dissolve, however, in much strong ammonia.

Compounds.—Xanthine forms a white crystalline sulphate of the composition $C_5H_4N_4O_2,H_2SO_4,H_2O$. A nitrate of a yellow colour is obtained by gentle evaporation to dryness of a nitric acid solution; this consists of delicate crystals, and becomes violet red on heating, but if overheated the mass readily carbonises. It also furnishes the hydrochlorate $C_5H_4N_4O_2+HCl$. The silver compound precipitated from an ammoniacal solution has the composition $C_5H_4N_4O_2+Ag_2O$. The nitrate of silver compound is soluble in nitric acid and recrystallises therefrom in needles; it loses nitric acid and silver by much washing with water. In this respect it differs from the corresponding hypoxanthine silver nitrate compound.

Decomposition products.—Rheineck obtained xanthine from uric acid by deoxidation with sodium amalgam thus:

$$C_5H_4N_4O_3-O=C_5H_4N_4O_2,$$

but attempts to consummate the converse of this reaction have not been successful. By a continuation of the above process of reduction Rheineck also states to have obtained hypoxanthine ($C_5H_4N_4O$). Thudichum, in his work on the urine, is not disposed to admit the close relationship thus apparently existing between these three bodies, and for this reason—that while all three yield parabanic acid ($C_3H_2N_2O_3$), by continued oxidation with nitric acid, yet only uric acid yields alloxan ($C_4H_2N_2O_4$) as an antecedent substance. Referring, however, to the structure formula I have given above to uric acid, this admits of explanation in some measure, as is presented below:—



In the formulæ for xanthine and hypoxanthine, H,HO and H,H take the place of the groups HO in uric acid.

Quantity of Xanthine excreted.—Thudichum records a case of albuminous urine where from 0·84 to 1·12 grm. of xanthine was excreted during the twenty-four hours.

Hypoxanthine, $C_5H_4N_4O$.

This substance was discovered by Scherer in the spleen, and subsequently in the blood of persons suffering from leukocythæmia, when it is also accompanied by leucine. The base described by Strecker under the name of 'sarkine,' and obtained from the extract of flesh, is the same substance. Hypoxanthine, moreover, occurs in the thymus and thyroid glands, in the brain, liver, kidneys, and other organs, but does not appear to be a normal constituent of urine. In leukocythæmia and diseases of the liver and kidney, it appears in that fluid.

Method of Preparation.—It may be extracted from muscular tissue, the brain, or the heart of the ox, &c. &c., by making water extracts and subjecting them to the processes described under 'Xanthine.' Its hydrochlorate being more soluble than the corresponding salt of xanthine, it may generally be separated from that substance by a process of fractionation carried out with the mother liquors. Or it may be separated from uric acid and xanthine by dissolving in dilute sulphuric acid, boiling, filtering whilst hot, and precipitation of the filtrate by nitrate of mercury. The filtrate from this precipitate gives, with an ammoniacal solution of argentic nitrate, a compound which, on decomposition with sulphuretted hydrogen, yields the free base. Or it may be obtained, as already described, from xanthine by reduction with sodium amalgam.

Properties and Characters.—Hypoxanthine is a white powder consisting of needle-like crystals, which are nearly insoluble in cold water, and which deposit in crusts on concentration of its aqueous solutions. Its general reactions are like those of xanthine, to which substance, as already stated, it is chemically closely allied. This connection is rendered more certain by the fact that it admits of transformation into that substance by oxidation with fuming nitric acid, and treatment of the nitro-product thus obtained with ferrous sulphate and ammonia, thus:—

$$2(C_5H_4N_4O) + 2(NO_2) + 3O = 2(C_5H_3(NO_2)N_4O_2) + H_2O,$$

and

$$C_5H_3(NO_2)N_4O_2 + 5H = C_5H_4N_4O_2 + 2H_2O + N.$$

Compounds of Hypoxanthine.—The hydrochlorate $C_5H_4N_4O,HCl + H_2O$, crystallises in colourless plates, and is somewhat decomposable by much water.

The platinum salt $2(C_5H_4N_4O,HCl).PtCl_4$ is also crystalline, and is more soluble in hot than in cold water.

A nitrate and sulphate are also known, as well as the compounds $C_5H_2BaN_4O + 2H_2O$; $C_5H_2Ag_2N_4O + H_2O$, and $C_5H_4N_4O + AgNO_3$. This latter salt is very characteristic, and may be obtained by precipitation of an aqueous solution of the base with nitrate of silver. It readily dissolves in somewhat strong boiling nitric acid, and is reprecipitated on cooling, in beautiful needles of a definite composition.

Other chemical Relations of Hypoxanthine.—Hypoxanthine is considered to be closely related also to guanine (a well-known constituent of guano, and sometimes found in the human liver and spleen). The two substances present many characters and general reactions in common. Guanine is, however, $C_5H_5N_5O$, and is sometimes regarded as amidated hypoxanthine; moreover, just as hypoxanthine yields xanthine by oxidation and subsequent reduction of the nitro-compound with ferrous sulphate, so also guanine under such treatment yields xanthine.

By one process of oxidation, guanine yields parabanic acid, guanidin, and carbonic anhydride, thus:—

$$C_5H_5N_5O + H_2O + 3O = C_3H_2N_2O_3 + CH_3H_5 + CO_2;$$

and by another milder process of oxidation, employing potassic permanganate, guanine is converted into urea, oxalic acid, and oxyguanin.

The great interest of these bases consists in their relation to the urea bodies and uric acid on the one hand, and their common derivation by metamorphosis of albuminous compounds on the other hand.

The other chemical relations of guanine are given below.

Guanine, $C_5H_5N_5O$.

This substance is so chemically interesting, that, although it is doubtful whether it ever occurs in urine, it deserves some mention here. Scherer states to have found it in the liver and pancreas, but the detection depended for its interpretation rather upon mere test-tube experiments than upon analysis.

Guanine occurs in the excrements of spiders, the crayfish, the scales of fishes, &c. &c. Peru guano furnishes about a half per cent. of guanine, and other kinds yield it also in smaller amount.

Method of Preparation.—It may be obtained by boiling guano with milk of lime for 24 or 30 hours, until, in fact, ammonia ceases to be evolved. The insoluble deposit is then repeatedly extracted with boiling water, and the united extracts neutralised with hydrochloric acid and concentrated. After some time a reddish precipitate occurs; this consists of a mixture of guanine and uric acid. It is isolated and extracted with boiling hydrochloric acid, which, while it leaves the uric acid almost entirely undissolved, takes up the guanine, and on cooling of the filtrate the hydrochlorate is deposited in crystals. From the hot aqueous solution of this salt, the pure base is obtained by precipitation with ammonia.

General Properties of Guanine.—Guanine is a white powder, insoluble in water, alcohol, and ether, and quite insoluble in acetic acid. With strong acids it forms crystallisable salts, and with the chlorides of mercury, cadmium, zinc, and platinum, the hydrochlorate yields double salts.

Kerner found[1] that, when introduced into the human stomach, it increases the amount of excreted urea.

The chemical decompositions of this base have been already described under 'Hypoxanthine,' and it is only necessary here to name the chief compounds of guanine. They are as follows ;—

Nitroguanine, $C_5H_4(NO_2)N_5O$, and a nitrate of this, $C_5H_4(NO_2)N_5O,HNO_3$.
The hydrochlorate, $C_5H_5N_5O,HCl + H_2O$.
" nitrate, $C_5H_5N_5O,HNO_3$.
" " of silver compound, $C_5H_5N_5O,AgNO_3$.
" double platinum salt, $2(C_5H_5N_5O,HCl) + PtCl_4 + H_2O$.
And the mercury compound, $2(C_5H_5N_5O,HgCl_2) + 5H_2O$.

Diagnosis of Bases allied to Xanthine.—Thudichum, in his work on the urine already mentioned, gives an interesting and important diagnosis of the chief reactions of bases of the xanthine group, which, with his permission, I here reproduce ;—

Xanthine, hypoxanthine, and guanine resemble each other :—

'(1) By their solubility in dilute warm nitric acid.
(2) Their precipitation from this solution by argentic nitrate.
(3) The solubility of this silver compound in much warm moderately dilute nitric acid.

But they differ by :—

(4) Hypoxanthine silver nitrate being quickly deposited in crystals on cooling.

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[1] Kerner, *Ann. Chem.* 103 (1857) 219.

(5) Xanthine silver nitrate being deposited from a similar solution only after long standing.

(6) Guanine silver nitrate seems to be deposited at a period later than hypoxanthine and earlier than xanthine.

They further resemble each other:—

(7) By being precipitated as silver compounds free from nitric acid by a slight excess of ammonia added to the nitric acid solution just described.

(8) By the complete solubility of these silver compounds in a large excess of concentrated caustic ammonia.

(9) By the reappearance of the silver compound when the large excess of ammonia is allowed spontaneously to evaporate or is expelled by heat.'

Kreatine, $C_4H_9N_3O_2$.

Kreatine was discovered in the juice of flesh by Chevreul. It is in particular a constituent of working muscles, such as the heart of the ox, which contains as much as 1·3 per mille. According to Gregory, a pound of human flesh yields about 5 grains of kreatine, or according to Thudichum, 0·67 per mille; the flesh of fowls 3·2 per mille, and that of codfish 0·9 to 1·7 per mille.[1]

Thudichum further relates that the flesh of an ox fed on meat during 200 days at the Anatomical Institution of Giessen did not yield more than one-tenth as much kreatine as was obtained from the flesh of wild foxes. This and other considerations seem to indicate that kreatine is a product of change produced in muscles by the influence of motion: that it is an excretory product there can be little doubt, as we shall presently see when its chemical relations to urea and other bodies are described.

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[1] See Thudichum's work on the Urine, p. 133.

In the blood it appears to become changed into urea and kreatinine; but whether it occurs in normal urine is a matter of doubt, because, although it may be found accompanying kreatinine in urine, it is not certain whether the operations involved in its detection are not sufficient to produce it from that substance.

Method of Preparation.—Kreatine is best prepared from ox heart, fowls' flesh, pigeon's flesh, or beef, by freeing the tissue as far as possible from fat, then mincing it, and extracting repeatedly with water. The extract so obtained is heated to about 60° or 70° C., when the albuminous parts held in solution coagulate and carry down with them the myochrome (or colouring matter of muscles). The mixture is then filtered, first through a linen cloth and afterwards through paper, and freed from phosphoric acid and certain coloured matters by precipitation with excess of baryta water. The strongly alkaline solution must then be filtered, and the filtrate concentrated to a syrup and allowed to spontaneously evaporate, by which means a crystalline crop of the base is obtained. Or the syrup may be precipitated with basic acetate of lead, and the filtrate freed from excess of the reagent by means of sulphuretted hydrogen. The ultimate filtrate on concentration and spontaneous evaporation yields crystals of kreatine. These may be purified by re-dissolving them in hot water, and boiling with a little animal charcoal, then filtering and again crystallising.

General Properties and Characters.—Thus obtained, kreatine forms colourless brilliant prismatic crystals of specific gravity 1·34-1·35, and containing a molecule of water which may be dispelled at a temperature of 100° C. Cold water dissolves only about 1·34 per cent. of kreatine, but the substance is readily soluble in boiling water. It is insoluble in absolute alcohol and in ether. The aqueous solution has a neutral reaction and a bitterish taste. Kreatine will not neutralise even dilute acids.

Compounds.—The hydrochlorate, $C_4H_9N_3O_2,HCl$, may be obtained in colourless, well-defined crystals, as may also the corresponding sulphate, $2(C_4H_9N_3O_2),H_2SO_4$, by the evaporation of equivalent quantities of the base and the acids in vacuo, or at a temperature below 30° C.

The nitrate, $C_4H_9N_3O_2,HNO_3$, is obtained in brilliant crystals by passing nitrous acid gas into a mixture of kreatine and water; the kreatine is thus dissolved, and after some time the nitrate is formed and deposited.

Chemical Decompositions and Relations of Kreatine.—When kreatine is boiled with excess of a strong solution of baryta water, it suffers decomposition, and in the first stage of the process sarkosine ($C_3H_7NO_2$) is formed, while ammonia and carbonic anhydride are evolved, but these latter probably result from a secondary change consisting of the decomposition of urea, which substance may be obtained from the solution; thus:—

$$C_4H_9N_3O_2 + H_2O = CH_4N_2O + C_3H_7NO_2.$$

On the other hand, if kreatine be boiled with strong solutions of hydrochloric, sulphuric, nitric, or phosphoric acid, it loses the elements of water and is transformed into kreatinine thus:—

$$C_4H_9N_3O_2 = C_4H_7N_3O + H_2O.$$

When kreatine in water is boiled with mercuric oxide, it yields an oxalate of a basic substance called methyluramine ($C_2H_7N_3$), and the same base may be produced by substituting sulphuric acid and peroxide of lead for the oxide of mercury.

Methyluramine yields methylamine (CH_5N) by treating with alkalies, and this substance is also produced by treating kreatine itself with soda-lime. As kreatine, when subjected to other processes of decomposition, yields methyl-parabanic acid; methyluramine may be regarded as the residue of a compound of urea and methylamine, resulting from the abstraction of water, thus:—

$$C_2H_7N_3 + H_2O = CH_4N_2O + CH_5N.$$

The other decompositions of kreatine are not of peculiar interest for the purposes of this work.

Kreatinine, $C_4H_7N_3O$.

Kreatinine was first obtained (in the form of an unknown compound with zinc chloride) by Heintz and Pettenkofer from human urine, and afterwards Liebig established the simultaneous presence of kreatinine and kreatine in the juice of all kinds of flesh from vertebrate animals. But inasmuch as Heintz and Liebig both subsequently determined that kreatine is formed at the expense of kreatinine (as already explained under 'Kreatine'), it remains doubtful whether kreatine exists at all naturally in the body. Liebig also found that in urine which has undergone putrefaction, the kreatine becomes changed and disappears, while the kreatinine is not attacked.

Kreatinine, then, is excrementitious, like to and related to urea, and it is accompanied in the juice of flesh and in the urine with kreatine, but the latter may possibly be derived entirely from the former.

Method of Preparation.—Kreatinine is best prepared from urine by treating it with milk of lime, neutralisation of the filtrate with acetic acid, evaporation, and removal of the salts which are separated on crystallisation. The ultimate syrupy mother liquor gives on addition of a neutral solution of chloride of zinc, and standing for a few days, a deposit of kreatinine in combination with that salt, $C_4H_7N_3O,ZnCl_2$. This, however, is not unmixed with kreatine, and to purify the preparation the deposit is dissolved in water at 100° C., and decomposed with hydrated oxide of lead. In this way an oxychloride of lead is produced, together with oxide of zinc, both of which are insoluble, while the kreatinine and kreatine pass into solution. On evaporating this to dryness, and extracting with much absolute alcohol, the kreatinine dissolves, while the kreatine remains undissolved.

The same result may be obtained in a more direct way by evaporating the neutralised filtrate resulting after the milk-of-lime treatment of urine, to dryness, and extraction of the residue with alcohol which leaves kreatine undissolved.

The extract so obtained gives the zinc compound, with a few drops of the neutral chloride of zinc solution, and after it is fully deposited (in the course of 48 hours or so) it may be decomposed as before described. Neubauer found that the zinc salt obtained as above was pure enough, after washing with alcohol, to be weighed.

Kreatinine may be also obtained, as already described, by boiling kreatine with strong hydrochloric acid, which process yields the hydrochlorate, and this, by decomposition with hydrated oxide of lead, gives the free base.

It may also be obtained from urine in a way different from that sketched above. Fresh urine is fully precipitated with neutral lead acetate and the filtrate concentrated and freed from lead by sulphuretted hydrogen. On adding a solution of corrosive sublimate to the mother liquor, a white double compound of kreatinine with mercuric chloride is precipitated, and this, by suspension in water and decomposition with sulphuretted hydrogen, gives hydrochlorate of kreatinine, which may be crystallised out of the solution after concentration, &c.

Kreatinine may be purified by re-crystallisation from alcohol containing a little animal charcoal.

General Characters and Properties.—Kreatinine crystallises in oblique rhombic prisms. Water dissolves about 8·7 per cent. at 15° C., and in hot water it is much more soluble. Cold absolute alcohol dissolves about 1 per cent. of kreatinine, but it is readily soluble in hot alcohol.

The watery solution is of an alkaline character and taste. It is precipitated by argentic nitrate, giving a mass of small delicate needles of a double compound, soluble in hot water, and crystallising out again on cooling.

Compounds of Kreatinine. — The hydrochlorate $C_4H_7N_3O,HCl$ may be obtained, as described above, from urine. It may be also produced in an anhydrous state by passing dry hydrochloric acid gas over dry kreatine

100° C. This salt is soluble in hot alcohol, and is crystalline.

A crystalline sulphate, $C_4H_7N_3O,H_2SO_4$, is also known. By evaporating a mixed solution of kreatinine hydrochlorate with one of platinic chloride, rosy prismatic crystals of a double salt are obtained, containing 30·95 per cent. platinum.

The chloride of zinc compound has the formula $2(C_4H_7N_3O)ZnCl_2$, and crystallises in large granules, warts, or needles. It is not very soluble in cold water or in strong alcohol.

With the salts of copper, kreatinine forms a blue crystallisable compound.

Chemical Relations and Decompositions.—The general relations and changes of kreatinine have been already described under 'Kreatine,' but the following facts may also be noted here:—

When treated in water with nitrous acid gas, an effervescence occurs, and the nitrate of a weak base of the composition $C_6H_{10}N_6O_3$ is formed. When this is heated to 100° C. with hydrochloric acid, oxalic acid, chloride of ammonium, and a base (perhaps $C_4H_4N_2O_3$) are produced.

When boiled with potassic permanganate, kreatinine is decomposed, yielding methyluramine oxalate.

$$2C_4H_7N_3O + H_2O + 5O = 2(C_2H_7N_3)C_2H_2O_4 + 2CO_2.$$

Physiological and Pathological Quantity of Kreatinine in Urine.—Calculating all the kreatine and kreatinine obtained from the urine as kreatinine, Thudichum determined the amount excreted in twenty-four hours at about 0·745 grm., and Neubauer found from 0·6 to 1·3 grms.

Of the quantity excreted in disease, Thudichum writes, 'The quantity of kreatine, together with that of kreatinine, might serve to indicate the intensity of any spasmodic or convulsive action.'

It appears that the quantity of kreatine and its congener contained in the muscles stands in a sort of relation to the quantity of fat deposited in the body, or rather to those causes which, by their operation, determine the deposition of fat. The more fat the less kreatine is there; and this is quite appreciable if we bear in mind that the mass of evidence goes to show that kreatine and kreatinine are products of change induced through muscular exertion: if so, then the amount depends upon the degree of exertion, and the amount of fat deposited in the body will be in an opposite proportion.

Sarkosine, $C_3H_7NO_2$.

Although this substance has never been obtained direct from the fluids or tissues of the body, it is of interest as a product of decomposition of kreatine.

We have seen that when kreatine is boiled with baryta water it splits up into sarkosine and urea, and it may thus be obtained by continuing the process until all the urea is decomposed into carbonic anhydride and ammonia, and crystallising it from the residual filtered solution, after freeing this from excess of barium by means of carbonic acid.

It may be purified by conversion into the sulphate and decomposition of this with carbonate of barium.

Properties and Characters.—Sarkosine crystallises in transparent, colourless, right rhombic prisms. It is freely soluble in water, sparingly soluble in alcohol, and quite insoluble in ether.

The crystals melt at a little above 100° C., and sublime unchanged. The aqueous solution has no action on vegetable colours. A solution of sarkosine gives, with one of cupric acetate, an intense blue colour; and, on evaporation of the mixture, a dark blue crystalline double salt is obtained.

If to a solution of mercuric chloride a crystal of sarkosine be added, a double crystalline salt is formed throughout the mass.

Chief Compounds of Sarkosine. — The sulphate, $2(C_3H_7NO_2)H_2SO_4,H_2O$, crystallises in colourless cubes, and is obtained by mere treatment of sarkosine with sulphuric acid in equivalent quantities, and crystallisation.

When a solution of the hydrochlorate is heated with platinic chloride and allowed to spontaneously evaporate, large flattened yellow octohedral crystals of a double salt separate; this has the composition expressed by $2(C_3H_7NO_2,HCl).PtCl_4,2H_2O$, and loses its water of crystallisation at 100° C.

Chemical Relations and Decompositions of Sarkosine. —Sarkosine is isomeric with ælanine, carbamic ether (urethane), and lactamide, but quite distinct from all these substances in its properties; chiefly by its insolubility in ether and alcohol.

Strecker regarded sarkosine as methyl-glycocine, $C_2H_2(CH_3)(H_2N)O_2$, and an experimental support was given to this view by Volhard, who prepared sarkosine synthetically by heating methylamine in excess with chloracetic acid in sealed tubes to 130° C.

$$C_2H_3ClO_2 + CH_5N = HCl + C_2H_2(CH_5N)O_2.$$

The connections between sarkosine, kreatine, kreatinine, xanthine, hypoxanthine, guanine, and uric acid and urea, are therefore pretty well established in many points; but this is a subject which admits of and calls for extended investigation. It will be seen that the structural formula given to uric acid in the section on that subject becomes more intelligible in the light of other results given in subsequent places.

Hippuric Acid, $C_9H_9NO_3$.

This substance was discovered as a chemical individual present in the urine of cows by Rouelle, in 1784; he also showed that during the putrefaction of the urine it decomposed. About 1829 Liebig analysed it, and Keller showed that when benzoic acid was taken into the stomach, hippuric acid appeared in the urine in increased quantity. Subsequently, Dessaignes effected the synthesis of this acid from benzoic acid and glycocine.

That hippuric acid is a normal constituent of human urine appears to be proved beyond doubt, while it is a regular ingredient also of the urine of herbivorous animals; it is, moreover, present in guano.

Method of Preparation.—The fresh urine of cows is treated with milk of lime, boiled, filtered from the precipitated phosphates, &c., and the filtrate treated with hydrochloric acid to neutralisation. On concentration and a further addition of hydrochloric acid, brown crystals of hippuric acid are gradually deposited. As thus obtained, the acid may be purified by re-dissolving in water and decolorisation by means of chlorine gas.

In this way the colouring matter associated with the crystals is oxidised and rendered soluble, and by crystallisation of the solution, pure hippuric acid is obtained in long, colourless, transparent needles.

Or the impure acid may be directly obtained from the fresh urine of cows fed upon grass by addition of a considerable excess of hydrochloric acid; Kraut in this way obtained more than one pound of the crude product from 120 pounds of urine.

It is best obtained from human urine as follows:—While still fresh, the urine is treated with milk of magnesia, filtered, and the filtrate concentrated to a syrup. The product has then to be strongly acidified with hydrochloric acid, and the mixture extracted with ether. By distillation of the ethereal extract, hippuric acid is obtained in a more or less impure state, and may be purified as above described, or by heating its aqueous solution with animal charcoal, filtering, and re-crystallising. Or the acid may be prepared synthetically by heating equivalent quantities of benzoic acid and glycocine in sealed glass tubes at 160° C. A similar result is obtained by heating monochloracetic acid and benzamide, also in sealed tubes, at 155° C., when the following reaction occurs:—

$$C_2H_3ClO_2 + C_7H_5(H_2N)O = C_9H_9NO_3 + HCl.$$

Properties and Characters of Hippuric Acid.—Pure hippuric acid crystallises from water in prisms, but from alcoholic solutions it is deposited in granules of a crystalline nature. It is but slightly soluble in cold water (1 in 400), but is soluble in boiling water and alcohol; quite or almost insoluble in ether, but soluble in sodium phosphate solution. Its aqueous solution presents an acid character to test paper. Hippuric acid is monobasic, and forms a number of clearly-defined salts.

Compounds of Hippuric Acid.—The salts of the alkalies and of magnesium are very soluble in water, and crystallise with difficulty. Acid salts of potassium and sodium may be obtained. Calcium hippurate, $Ca(C_9H_8NO_3)_2 3H_2O$, is obtained by the decomposition of calcic carbonate with hippuric acid. It is soluble in water, and crystallises in rhombic prisms.

Hippurate of lead, $Pb(C_9H_8NO_3)_2$, is also somewhat soluble in water. It is deposited in curds from strong solutions, but from more dilute solutions it crystallises in tufts of silky needles, containing $2H_2O$, and these gradually change into broad quadrangular plates, containing $3H_2O$. There is also a basic hippurate of lead and salts of mercury, silver, iron, cobalt, nickel, copper, and zinc.

When to a solution of hippuric acid in concentrated nitric acid there is added an equal bulk of sulphuric acid, meanwhile avoiding any considerable rise in temperature, nitro-hippuric acid, $C_9H_8(NO_2)NO_3$, is produced, and is gradually deposited from the solution on dilution with much water. By boiling with sulphuric or hydrochloric acid, nitro-hippuric acid is converted into nitrobenzoic acid and glycocine. On the other hand, when nitro-benzoic acid is taken internally, it reappears in the urine as nitro-hippuric acid, having combined in the system with glycocine.

Decompositions and Chemical Relations of Hippuric Acid.—Hippuric acid melts at a gentle heat, and at about 260° C. decomposes with an appearance of ebullition: by distilling in this manner it yields benzoic acid, and a red oil containing benzo-nitrite; hydrocyanic acid and ammonia are also produced, while a mass of charcoal is left behind.

It has already been stated that by boiling with acids it is resolved into benzoic acid and glycocine, thus :—

$$C_9H_9NO_3 + H_2O = C_7H_6O_2 + C_2H_5NO_2.$$

Alkalies produce a similar result with the formation of benzoates of the alkalies; and it is also stated that certain ferments are capable of initiating and carrying out a similar decomposition, particularly in the presence of alkalies. The decomposition of the acid in putrefying urine is explained in the way last mentioned. From the behaviour of benzoyl chloride with oxide of zinc it is conjectured that hippuric acid is benzoyl glycocine, $C_2H_4(C_7H_5O)NO_2$, and this view derives support from the fact that, when boiled with peroxide of lead, a solution of hippuric acid yields carbonic anhydride and benzamide, thus :—

$$C_2H_4(C_7H_5O)NO_2 + O_3 = H_2O + 2CO_2 + (C_7H_5(NH_2)O).$$

When hippuric acid is acted upon by nitrous acid, the following reaction occurs :—

$$2(C_9H_9NO_3) + N_2O_3 = 2(C_9H_8O_4) + 4N + H_2O.$$

That is to say, benzoglycolic acid and nitrogen are formed, and it was upon this basis that Strecker regarded hippuric acid as amidated benzoglycolic acid.

This benzoglycolic acid crystallises in rhombic prisms, and is easily soluble in alcohol and ether, but not very soluble in water. It also forms the calcium salt $Ca(C_9H_7O_4)_2$, which is crystalline.

When heated with dilute acids, benzoglycolic acid splits up into benzoic acid and glycolic acid, thus :—

$$C_9H_8O_4 + H_2O = C_7H_6O_2 + C_2H_4O_3.$$

From the foregoing detailed facts, hippuric acid is sometimes regarded as benzoyl glycocine and sometimes as amidated benzoglycolic acid.

Physiological Quantity of Hippuric Acid.—Not only benzoic acid, but also benzoic ether, benzoyl hydride, cinnamic acid, and in short, a large number of benzene derivatives, split up when introduced into the animal economy, the benzoyl radical reappearing in combination with glycocine in the urine as hippuric acid. In consequence, the nature of vegetable food has a direct influence upon the quantity of hippuric acid present in the urine. Greengages, which contain much benzoic acid, therefore, when taken as food, materially increase its amount. From the fact that hippuric acid seems to be a constant ingredient in urine, it appears necessary to assume that albuminous substances in the body are capable of furnishing the benzoic acid necessary to give rise by combination with glycocine, to the production of hippuric acid. The source of the glycocine is still problematical.

Reviewing a mass of evidence based upon the researches of Ure, Keller, Hallwachs, Ducheck, Proust, and Kühne, in addition to his own, Thudichum writes[1] relative to the transformation of benzoic into hippuric acid in the economy as follows :—

'On the whole, the experiments show that the transformation is probably effected in the intestinal canal ;

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[1] Work on the Urine. 1877 edition, p. 154.

that the bile is not essential to it; that other products of the decomposition of the food in the intestinal canal can furnish the glycocine, and that the blood by itself does not furnish the glycocine, or allow its combination with benzoic acid to take place within the limits of the circulation.'

Hallwachs determined the quantity of hippuric acid contained in 24 hours' urine at 1 grm., while Weissmann arrived at a larger figure, but it is probable from his method of investigation that the hippuric acid he obtained was contaminated with other substances. Bence Jones, in a number of experiments, arrived at a mean figure less than one-half of that given by Hallwachs, and showed that the quantity was increased after taking food. Thudichum found much larger quantities,—a fact which he explains by pointing out possible losses in the method of Bence Jones and other investigators. Hallwachs' determination may therefore be taken as tolerably near the truth. It must not be forgotten, however, that the amount of hippuric acid varies with the nature of the food, and is particularly increased when greengages, plums, blackberries, and other fruits are eaten.

The hippuric acid present in urine is supposed to exist, partly at least, as sodium salt; but when the quantity is great, or when the urine contains much free acid, hippuric acid is deposited in the free state.

It should also be stated that, accompanying hippuric acid, Thudichum met with benzoic acid in a number of cases, and according to him, under such conditions as negative the derivation of it from hippuric acid.

According to certain authors, the excretion of hippuric acid is increased in febrile affections and diabetes, but as a matter of fact the quantity appears to depend more upon the nature of the food than upon the disease.

Reducine, $C_6H_{11}N_3O_4$.

In a recent publication,[1] Thudichum details the method by which he succeeded in isolating what he considers to be a new constituent of human urine. This matter will be best understood by briefly indicating the exact way in which he obtained it.

The urine was acidified by sulphuric acid, and fully precipitated by a nitric acid solution of phosphomolybdic acid. The precipitate was washed with water slightly acidulated with sulphuric acid, and then decomposed by boiling baryta water in excess, filtered, and the filtrate freed from excess of uncombined barium by carbonic anhydride. This filtrate, when concentrated, deposited urate of barium, and was shown to contain much urochrome, as evidenced by the decomposition products which it yielded. It was therefore subjected to successive precipitations with neutral lead acetate, basic lead acetate, and an ammoniacal solution of the latter reagent. It was from these precipitates by decomposition with sulphuretted hydrogen that Thudichum obtained urochrome and xanthine. The filtrate from the lead precipitates was freed from lead by sulphuretted hydrogen, and was then found to contain kreatinine and the new body *reducine*. These were separated by evaporation to dryness and extraction of the residue with boiling absolute alcohol. In this way the kreatinine was removed, and an insoluble combination of reducine with barium remained undissolved.

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[1] *Report Medical Officer of the Privy Council.* New Series, No. vi. p. 211, 1875.

This barium salt was soluble in water, and left barium carbonate when ignited. A solution of the salt in water when acidified with nitric acid and treated with silver nitrate, gave a white precipitate, which blackened almost immediately. Hence Thudichum named the new body *reducine.*

The barium salt dry at 100° C., showed on analysis the following percentages:—

C.	27·092
H.	4·282
N.	15·850
Ba.	25·400
O.	27·376

And from these the provisional formula at the head of this article was calculated out.

Indigogen, C_8H_6NO, *and Urrhodinogen.*

In 1845 Heller[1] found in the urine a yellow substance, termed by him uroxanthine, which by treatment with acids in the warm yielded a blue colouring matter, uroglaucine, and a red one, urrhodine. Later on, Kletzinsky proved the identity of the blue substance with indigo blue, and erroneously asserted the identity of the red colour with indigo red. This subject attracted from time to time a number of workers, and so vast has become its literature that it is impossible, as it is equally unprofitable also, to follow it in any detail. Suffice it to say, that about 1854 Schunck[2] obtained from indigoferæ a principle resolvable by acids into indigo blue on the one hand and a sort of glucose on the other hand, as follows:—

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[1] *Archiv. für Chemie und Microsc.* 1845.

[2] *Manchester Memoirs*, 1855, vol. xii. p. 177.

$$\overset{\text{Indican.}}{C_{26}H_{33}NO_{18}} + H_2O = \overset{\text{Indigo Blue.}}{C_8H_5NO} + \overset{\text{Indiglucin.}}{3C_6H_{10}O_6}.$$

Subsequently, by suitable treatment, he claimed to have demonstrated the identity of Heller's and Kletzinsky's uroxanthine with his indican.

Since then (1864) Thudichum controverted this doctrine of the glucoside nature of uroxanthine; but to-day, while Thudichum is not alone in his views, a number of other physiological chemists endorse the more popular notion already alluded to, and which is supported by Jaffé.

Thudichum's view has been supported by Kingzett and Hake,[1] who, writing of indican, say: 'Its presence in the urine at any time is extremely doubtful, for in the first place no such substance has ever been isolated from urine, and in the second place, when that blue colour is obtained which is supposed to be characteristic of indigo blue, and referable to indican, side by side with it, *sugar is not produced.* When a solution is obtained which exercises a reducing action on Fehling's copper solution,[2] there is every reason to believe the case abnormal in some respect. When urine is treated with its own volume of hydrochloric acid, a blackish precipitate falls on standing, and this, after extraction with dilute acid and then with absolute alcohol, is said to leave indigo blue upon the filter. We have rarely met with cases where any blue is obtained, and when it has been obtained it has amounted to little more than a stain. But it will be evident that in any case it is not justifiable to speak of indican as a never-failing constituent of urine. Further, the name should no longer be retained, for if indican be a glucoside, and if the blue colour from urine be unattended with sugar, then at least the substance in the urine cannot be indican.'

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[1] *Quarterly Journal of Science*, January 1877.

[2] See Virchow's experiments (Virchow's *Archiv.* 6, 259).

Method of Preparation of Indigo blue.—Heller's method is as follows. Fresh urine is precipitated by a hot solution of plumbic acetate, and the filtrate freed from lead by sulphuretted hydrogen, the excess of the latter reagent being expelled by boiling. The solution thus prepared is poured into an equal volume of pure concentrated hydrochloric acid, stirring in the meantime. The mixture generally becomes of a blue colour, and if only violet or red, no indigo blue will be obtained. Blue solutions, however, deposit, after admixture with an equal quantity of water and some twelve or more hours' standing, a copper-red coloured deposit, and this after twenty-four hours is separated by filtration, washed with water at 100° C., and finally with alcohol. When dried, it is extracted with ether so long as the ether extracts are of a red colour. This red matter is urrhodine, and of this more anon. The insoluble blue matter is extracted with alcohol of 0·83 to 0·90 sp. gr., so long as anything is dissolved, and from the filtered extracts indigo blue deposits on cooling in microscopical crystals, leaving the alcoholic mother liquor colourless.

Schunck's Method of obtaining Indigo blue from Urine is as follows:—

The urine is first precipitated with normal acetate, and then with basic acetate of lead, the deposits being removed. The nearly colourless liquid, freed from phosphoric and sulphuric and some hydrochloric acid, is now treated with ammonia, which causes a further lead compound to be precipitated, and when this is decomposed by an acid, the filtrate deposits, on standing, indigo blue. Indigo blue and urrhodine may also be prepared from urine which contains the necessary antecedent principles, by mixing with an equal volume of strong hydrochloric acid, after which the first-named bodies gradually deposit during the few ensuing days.

It is quite unnecessary to give the description of a number of other proceedings by which the same results are attained.

That the indigo blue and urrhodine are not derived from the yellow colouring matter of urine is certain, for the most colourless urine, such, for example, as the first urine in the reaction from cholera, yields the most indigo blue. Further, the very method (of precipitation with lead) of isolating indigo blue removes previously most of the colouring matter of the urine. Indigo blue is therefore derived from a colourless constituent of the urine or indigogen, C_8H_6NO (?).

On the other hand, urrhodine seems to have no relation to indigo red. When obtained from the ether extract of the mixture of indigo blue and itself by distillation, it forms an uncrystallisable brownish red resin, which is free from nitrogen. Thudichum calls the body which furnishes it by decomposition with the acid, urrhodinogen.

That it is free from nitrogen was proved by an analysis of Thudichum's, conducted on the principles described by Thudichum and Kingzett,[1] in which it showed 81·0 per cent. carbon, but no nitrogen.

This substance, urrhodine, when sublimed, yields a red vapour, which condenses into an amorphous red matter mixed with minute colourless crystals. It is very soluble in alcohol. Urrhodine, therefore, has probably never been obtained pure, but it is proved to have no relation to indigo red, and well deserves more exhaustive study.

Characters and Properties of Indigo blue from Urine.—Indigo blue (C_8H_5NO) from urine, when slowly precipitated from its solutions, or when obtained by sublimation, assumes the shape of minute irregular crystals. Its vapour has a violet red colour, and it is (when freshly precipitated) somewhat soluble in boiling alcohol, giving a solution with a characteristic spectrum.

It dissolves in fuming sulphuric acid to a blue colour.

The alcoholic solution of indigo and the solution of its sulpho-acid, are both rendered colourless by nascent hydrogen and other reducing agents. Moreover, when indigo blue is digested in a closed vessel with grape sugar and potash, it is also reduced to a colourless solution which becomes blue again by atmospheric oxidation. All these and other reactions prove the identity of the blue pigment obtained from urine with that obtained from plants. Indigo blue fuses at 288° C., and furnishes purple vapours. By destructive distillation it yields cyanide and carbonate of ammonium, aniline, and a peculiar empyreumatic oil.

It is insoluble in water, alcohol, ether, and the fixed and volatile oils, also in dilute acids and alkalies. By reduction, indigo blue yields, as already stated, white indigo, or indigogen, C_8H_6NO. Thus a mixture of ferrous sulphate and alkali effects this reduction in this way:—

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[1] *Journ. Chem. Soc.* 1876, ii. 363.

$$2(FeO,H_2O) + H_2O + 2C_8H_5NO = Fe_2O_3,2H_2O + 2C_8H_6NO.$$

Chemical Decompositions and Relations of Indigo blue.—By oxidation with a dilute solution of chromic acid, indigo blue yields isatin:—

$$2C_8H_5NO + O_2 = 2C_8H_5NO_2.$$

Fuming nitric acid gives indigotic or nitro-salicylic acid ($C_7H_5(NO_2)O_3$), and by a more prolonged action carbazotic acid (picric acid) ($C_6H_3(NO_2)_3O$) is produced.

There are other interesting decompositions and chemical relationships of indigo blue, to study which, however, would lead us too far away from the direct object of this work.

It may be worth while to add, that when indigo blue is reduced with tin and hydrochloric acid, it gives a yellowish brown powder, and this distilled with zinc dust, gives a thick oil, from which aniline may be removed, after which, by distillation with superheated steam, crystals of indol, C_8H_7N, are obtained.

In the Chapter on Albuminous Compounds it will be shown how Nencki obtained this same body from albumin, and in this way some sort of connection between indigogen in the urine and the digestion of albuminous compounds is established.

Quantity of Indigogen excreted.—The quantity of indigogen excreted in health is not easy to determine, nor has it been done satisfactorily. It is probably small. Schunck obtained from the urine of two individuals, over a period of some weeks, only one grain of indigo blue.

Jaffé has estimated the quantity of indigo blue obtained from twenty-four hours' human urine at 0·0045 to 0·0195 grm.; dog's urine gives more, and a yet greater quantity is obtained from urine of cows, while horses give apparently twenty-five times as much as man.

Thudichum and others have shown that in the early urine passed by patients recovering from cholera collapse, indigogen is present in unusually large quantities.

Pyrocatechin, $C_6H_6O_2$.

This substance was discovered in human urine by Müller and Ebstein. Baumann[1] has since shown that while it is a frequent ingredient of human urine, it is probably not a constant one. The same author shows that it occurs in the urine of horses, partly uncombined, and partly as a sulpho-compound.

It is obtained from urine, when present, by acidification, evaporation, and extraction of the residue with ether. On distillation of the ether a residue is obtained which gives the reactions of pyrocatechin. It is chiefly interesting as an ingredient of urine from its chemical relations to the decomposition products of indigo. Lautemann obtained it artificially by decomposing moniodosalicylic acid with an alkali; in this way oxysalicylic acid is first produced, and this, on heating, is resolved into pyrocatechin and carbonic anhydride, thus:—

$$(1)\ C_7H_5IO_3 + KHO = C_7H_6O_4 + KI.$$
$$(2)\ C_7H_6O_4 = C_6H_6O_2 + CO_2.$$

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[1] Pflüger's *Archiv.* 12 (1876) 63.

Pyrocatechin may be regarded as benzene in which two hydrogens are substituted by two hydroxyls. It behaves as a weak acid, and crystallises in white shining laminæ, melting at about 112° C., and volatilising above that temperature.

When present in urine which has been rendered alkaline, oxygen is absorbed from the air, and the urine darkens in colour.

Phenol-Sulphuric Acid, $C_6H_6SO_4$, *and Cresol-producing Substances.*

Although phenol is not an ingredient of human urine, as such, yet Städeler extracted it from human urine, as also from the urine of the horse and the cow. Quite recently Baumann[1] has established the presence of phenol-sulphuric acid in horses' urine, and he found the same compound in the urine of persons who had been treated medicinally with phenol. There seems also to exist, both in blood and urine, another compound, as yet unisolated, which may yield phenol.

In the same manner cresol, C_7H_8O, while it is not a normal ingredient of human urine, may be obtained as an educt therefrom under certain circumstances.

The Colouring Matters of Urine.

Under the name of urobiline Jaffé has described[2] a colouring matter which he first observed in the urine of fever patients. Although afterwards detected in all specimens of urine, it seems to be produced therefrom only by standing, and not as an original constituent. It has never been isolated nor analysed, but merely diagnosed spectroscopically, and named under the assumption of some connection possessed by it with a biliary colouring principle. The subject has attracted other workers, but the results obtained have only been productive of new incongruous names and considerable dissension. It will therefore be passed over without further comment.

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[1] Pflüger's *Archiv.* 13 (1876) 2 and 7.

[2] *Arch. Pathol. Anat.* 47, 405.

Omichyl-oxide was the name given by Scharling[1] to a principle which he extracted from urine as follows:—The urine was concentrated by freezing and removal of the ice, and extraction of the concentrated solution with ether. By distillation of the ether extract, and washing of the residue with water, urea was removed, and the colouring matter remained behind. Scharling further purified it by boiling with solution of potash, to decompose ammoniacal salts, and precipitation of the solution thus obtained with sulphuric acid. Omichyl-oxide was deposited in brown flocks.

Omichyl-oxide fuses in hot water to an oily body, which resinifies on cooling. It is soluble in ether, alcohol, and dilute alkalies.

Thudichum claims to have shown that the substance is not contained in the urine as such, but is a secondary product of the action of heat and hippuric acid upon the matter extracted by ether.

Urerythrine is a substance first described by Proust under the name of rosacic acid, and obtained from the lateritious deposits from urine. A number of chemists, and, in particular, Heller, have studied this substance; but while it has thus gained in synonyms, it remains an unanalysed substance. It is that body which is supposed to give to urine its fiery red colour, and which adheres to the deposits of urates when they occur. It is best obtained from these deposits by first dissolving out what is soluble in water, and finally extracting the urerythrine by warm absolute alcohol. It is re-obtained from the alcohol by evaporation at a temperature not exceeding 50° C. It possesses a characteristic spectrum, and does not often occur in healthy urine, but is a frequent abnormal constituent. Thus it commonly occurs in cases of acute rheumatism, pericarditis, pneumonia, liver diseases, lead poisoning, intermittent fever, typhus, and certain brain diseases.

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[1] *Ann. Chem.* vol. xlii. p. 265.

Under the name of *Urohæmatine*, and many other names ('only to be said on holidays'[1]), Proust, Scherer, Harley, Heller, Marcet, and many others have described matters identical, allied, or totally different, which, in their opinion, constituted the true colouring principles of urine. Thudichum has given an account of many of these researches, both in his Hastings Prize Essay of 1864, and more recently in his book on the urine which has been so often referred to. While recognising the merit of each labourer's results, he has for the most part explained these away or identified their products with purer and more distinct principles obtained by himself from urine. It is therefore proposed to give a brief summary of Thudichum's laborious researches, in full satisfaction of all knowledge relative to the colouring matters of urine.

Before doing so, however, it may be well to explain that Harley gave the name of urohæmatine to a red colouring matter which he obtained from urine, in token of its supposed derivation from the colouring matter of the blood, a supposition based upon the fact that, when ignited, this substance left an ash of ferric oxide.

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[1] Once pointedly observed by the *Lancet*.

The matter which Thudichum regards as the chief or exclusive colouring matter of urine, he terms urochrome, and references have been already made regarding it, particularly in the section on 'Reducine.' Thudichum pays special credit to Proust, who, so long ago as 1800, seems to have got nearer the truth about urinary colouring matter than any other worker before Thudichum, who was able to identify and explain most of Proust's products.

Methods of Preparation of Urochrome.—(1) One method has been already described while treating of reducine—viz., precipitation by a nitric acid solution of phosphomolybdic acid. This fact appears to indicate that urochrome has an alkaloidal constitution.

(2) Or the urochrome may be obtained by precipitating urine with neutral and basic lead acetates, decomposition of the precipitates with sulphuric acid, and precipitation of the filtrates with phosphomolybdic acid.

(3) Another method consists in saturating urine in the cold with baryta hydrate crystals, filtration, and precipitation of the filtrates with lead acetate and ammonia to perfection. The washed precipitate is decomposed with sulphuric acid, and the filtrate again treated with baryta water, the excess of which has then to be removed by means of carbonic anhydride. The concentrated filtrate is then treated with strong alcohol, which precipitates kryptophanate of barium and other

matters, after separation from which, urochrome is obtained by evaporation in a current of air.

To purify the urochrome obtained by any process, its aqueous solution should be shaken with freshly precipitated oxide of silver, which removes both hydrochloric acid and traces of a xanthine-like body. The silver which thus enters into solution with the urochrome is removed by sulphuretted hydrogen, and on evaporation of the ultimate solution urochrome is obtained in the form of an amorphous, yellow-coloured substance. In the above-described treatment with argentic oxide, care has to be taken not to use an excess, or otherwise it precipitates the urochrome also.

Properties of Urochrome.—Thudichum has not analysed the urochrome itself, but he has determined the following characters:—It is not only soluble in water, but also less soluble in alcohol and in ether, very dilute acids, and alkalies. The aqueous solutions decompose slowly when kept, with increase of colour to red, and deposition of flakes of a resinous character. This decomposition occurs to a greater extent during operations which employ heat. Acids, when boiled with urochrome, decompose it, giving rise to products to be hereafter described. With a watery solution of urochrome, nitrate of silver gives a gelatinous precipitate soluble in nitric acid; it is also precipitated by acetate and basic acetate of lead, acetate of mercury, and nitrate of mercury.

Decomposition of Urochrome.—When boiled with dilute mineral acids for a length of time, urochrome decomposes, and developes an intense odour. The resin which separates, and more particularly on addition of a further quantity of water, consists of a mixture of three substances, uromelanine, uropittine, and omicholine (mixed with omicholic acid). From the isolated resinous matter uromelanine may be obtained by stirring it with cold water, when it separates from the admixture as a brown powder. Or it may be obtained by extracting the mixture with alcohol, which leaves uromelanine undissolved. The red alcoholic solution is precipitated by water, and from the precipitate so obtained ether extracts omicholine and its accompanying omicholic acid, while it leaves more or less powdery uropittine undissolved. These primary decomposition products are liable to be accompanied by smaller quantities of secondary products.

Characters of Uromelanine.—It is insoluble in water, and but slightly soluble in alcohol; hot alcohol redeposits most of what it dissolves, on cooling. It is easily soluble in dilute alkalies, and re-precipitated therefrom by acids.

Thudichum gives to uromelanine the formula, $C_{36}H_{43}N_7O_{10}$, based upon the analyses of a large number of preparations. He also describes three silver compounds in which the silver stands to the molecule of uromelanine in the respective proportions 1 : 1, 3 : 2, and 5 : 3. There is also a barium salt, three calcium salts, three zinc salts, and a lead salt, the analyses of which Thudichum also gives in detail.

Incidentally he shows that uromelanine presents a remarkable similarity in composition, to the pigment of the choroidea, as is seen in the following comparisons :—

	SCHERER.	THUDICHUM.	
	Melanine of the eye.	Uromelanine.	Theory of Uromelanine.
C.	58·28	57·21	58·93
H.	5·72	5·74	5·86
N.	13·77	13·88	13·36
O.	22·03	23·17	21·85

Characters of Omicholine and Omicholic Acid.—To separate these, the mixture is treated with strong ammonia, and warmed, and the extract so obtained allowed to stand, and finally filtered from the resinous mixture of the two substances which is deposited. The final ammoniacal solution contains only omicholic acid, while the more insoluble oily and resinous substance is omicholine. The formula of omicholic acid is not yet decided; it is near $C_{15}H_{22}NO_4$, or $C_{16}H_{24}NO_4$. The formula of omicholine is somewhere about $C_{22}H_{38}NO_5$, or $C_{24}H_{44}NO_6$. Neither substance has been yet obtained in a finally pure condition.

Characters of Uropittine.—The final purity of this body also has not yet been ascertained, but the following analyses may be quoted as roughly indicating its composition:—

					Mean.
C.	60·30	59·90	—	—	60·10
H.	6·29	7·04	—	—	6·66
N.	—	—	10·44	10·50	10·47
O.	—	—	—	—	22·77

Thudichum has also made and analysed a silver compound of this body.

For further details about these various principles I must refer the reader to Thudichum's own work on the urine. He there gives full particulars and treats of their direct production by the decomposition of urine, and enters into considerations of their physiological and pathological bearings, besides describing the characteristic spectrum presented by the solutions of each body.

One of Thudichum's considerations must, however, be recorded here. He takes uromelanine with an atomic weight of 733, and points out that inasmuch as it is a cleavage product of urochrome and one attended by at least two others, the constitution of urochrome must be very complicated; so complicated, indeed, that in view of uric acid, urea, and other substances known to be waste products derived from albumin, it is impossible to regard urochrome as also a derivative of that substance. It hence arises that urochrome must be regarded as a product from the breaking up of hæmato-crystalline (the colouring matter of the blood; see Chapter on Blood), which has a constitution far more complex than that of albumin and presents an atomic weight above 13,000.

This line of thought, backed up by further investigations yet to be made, may ultimately lead to 'a new means of estimating the effects of the febrile process upon the organ of oxygenation, the blood-disc, or its ally the myochrome or red colouring matter of the muscles.'

Further Remarks on the Decomposition of Urine.—Thudichum gives the following synopsis showing the products obtained when urine is distilled with sulphuric acid:—

'A. Fixed coloured products:—

Insoluble in ether; all soluble in ammonia.	Uromelanine	Insoluble in alcohol.
	Uropittine	Soluble, sparingly, in alcohol.
	Urorubine	Soluble easily, in alcohol.
	Metauropittine	Soluble in alcohol.
Soluble in ether and alcohol.	Omicholine	Insoluble in ammonia.
	Omicholic acid	Soluble in ammonia.

B. Volatile products:—

Soluble in ether	Essential oil.
As sodium salts insoluble in ether	Acetic and formic acids.

This synopsis will illustrate and serve as a *résumé* of what has gone before, while it leads naturally to a few remarks about the volatile oil obtained in this way from urine.

Volatile Oil from Urine.—This is soluble in ether, and is extracted from the distillate by this solvent. It has a powerful urinous odour, a yellowish colour, and when heated with nitrate of mercury it gives a purple reaction. It does not change a solution of silver even on boiling, and is free from phenol and cresol.

Acetic and Formic Acids.

We have already had occasion to write of the production of acetic and formic acids during the decomposition of urine. When distilled from putrid urine they are accompanied by benzoic acid, and may be readily obtained on the application of ordinary processes. Thudichum has shown that there is a difficulty in effecting the separation of acetate and formiate of barium on account of the isomorphous crystalline state of these substances. He however estimated, from some determinations made with the distillates of urine acidified with sulphuric acids, that the daily excretion of acetic acid amounts to 0·288 grm. per day, and that this is accompanied by about 0·05 grm. formic acid. From these proceedings it is difficult to say whether these acids are exclusively obtained by decomposition of more complicated substances, or whether they ever occur in the form of salts in the urine.

According to Meissner, succinic acid is also a regular ingredient of urine.

Kryptophanic Acid, $C_5H_9NO_5$.

Kryptophanic acid, which was discovered by Thudichum[1] in 1869, is considered by him to be the normal free acid of human urine, and may be isolated therefrom by various means.

Methods of Preparation.—Urine is treated with excess of lime milk, filtered, and evaporated; the sulphate of calcium which it afterwards deposits is subsequently removed by filtration and the filtrate acidified with acetic acid, after which it is concentrated and allowed to crystallise. The mother liquor, when treated with four or five volumes of strong alcohol, throws down a bulky adhesive precipitate consisting of kryptophanate of calcium, which may be purified by re-dissolving in water and re-precipitation with alcohol. To complete the purification the aqueous solution of calcium salt is precipitated by a strong solution of lead acetate, and the precipitate, which is soluble in a great excess of the reagent, is dissolved by this means and the solution so obtained precipitated by alcohol. From the white lead salts thus produced, free kryptophanic acid may be obtained by decomposition with sulphuric acid, and may be then transformed into other salts as required.

Or the crude kryptophanates may be treated with an excess of copper acetate. This solution throws down a dirty green precipitate of the copper salt, and a further quantity may be obtained from the mother liquor by addition of alcohol. When the copper salt is decomosed in the presence of water with sulphuretted hydro-en, free kryptophanic acid passes into solution.

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[1] *Journ. Chem. Soc.* 23 (1870), 116.

Thudichum shows that kryptophanic acid is not de-omposed when urine is boiled with dilute sulphuric acid.

Chemical Properties.—Kryptophanic acid is a trans-arent, gummy, solid body, soluble in water in all pro-ortions, but less soluble in alcohol and even more in-oluble in ether. It decomposes the alkaline and earthy arbonates, forming corresponding salts.

An aqueous solution is precipitated by acetate of nercury and nitrate of silver, while solutions of the lkaline and earthy kryptophanates are precipitated by he acetates of lead, copper, and mercury, and by the itrates of mercury and silver.

Thudichum has shown that the determination of urea n urine by Liebig's method is interfered with to the xtent of 5 or 10 per cent. by the circumstance that ryptophanic acid is precipitated by nitrate of mercury.

If kryptophanic acid be considered as tetrabasic, then he salts analysed by Thudichum have, according to him, he general formula $C_{10}H_{14}M'_4N_2O_{10}$.

The salts are as follows :—

Lead salt	$C_{10}H_{14}Pb_2N_2O_{10}$
„ hydrated	$C_{10}H_{14}Pb_2N_2O_{10} + 2Aq$
„ basic	$2(C_{10}H_{14}Pb_2N_2O_{10})PbO$
Copper salt	$C_{10}H_{14}Cu_2N_2O_{10}$
„ with alcohol	$C_{10}H_{14}Cu_2N_2O_{10} + C_2H_6O$
Magnesium salt	$C_{10}H_{14}Mg_2N_2O_{10} + Aq$
„ dihydrated	$C_{10}H_{14}Mg_2N_2O_{10} + 2Aq$
Barium salt	$C_{10}H_{14}Ba_2N_2O_{10} + Aq$
„ tribasic	$C_{10}H_{13}ba'_3N_2O_{10}$
„ acid	$C_{19}H_{14}BaN_2O_9$
Calcium salt	$C_{10}H_{13}Ca'_3N_2O_9$
„ acid	$C_{10}H_{14}CaN_2O_9$
Cobalt salt acid	$C_{10}H_{14}CoN_2O_9$
„ basic	$C_{10}H_{12}Co_2N_2O_9$
Silver salt	$C_{10}H_{12}Ag_3N_2O$.

Carbonic Acid.

This substance is contained in urine to some slight extent, and according to Plauer the amount increases under the influence of febrile processes. Other observations seem to show that the amount rises and falls with urea, and considering what we know of the chemical changes occurring in the blood, there is little difficulty in comprehending this to be true.

The Inorganic Constituents of Urine.

Chlorine and the Chlorides.—Principal among the inorganic constituents of urine are the chlorides of potassium and sodium, these substances, like many others, being constant ingredients of foods.

The crystals, which are deposited from a concentrated solution of urine, consist of common salt sometimes mixed with urea ; but from still more concentrated solutions the phosphates of sodium and ammonium are also thrown down. The potassium salts, from their greater solubility, are found in the mother liquors, and may be precipitated in the ordinary way by means of platinic chloride.

Bischoff made a number of determinations of the daily amount of chlorine passed in the urine, and the following table, which is taken from Thudichum's book, exhibits his results :—

Adult man, living well, discharged . .	8·7	grms.
Woman, forty-three years of age, discharged	5·5	,,
Girl, eighteen ,, ,, ,,	4·5	,,
Boy, sixteen ,, ,, ,,	5·3	,,
,, three ,, ,, ,,	0·8	,,

Of course the amount of chlorine must vary with each individual according to a number of circumstances, such as the amount of food taken, the amount of chlorides contained therein, and so on. From some experiments made by Hegar it would appear that less chlorine is secreted during rest and sleep than under conditions of mental and bodily activity.

Barral seems also to have shown that chloride of sodium increases the elimination of the nitrogenous constituents of the urine. It further appears that in acute febrile diseases less chlorides are excreted than is usual, but it is curious to note that in diabetes the quantity appears to be increased. Indeed, Thudichum considers that the amount of chlorine in chronic cases of disease serves as a measure of the digestive powers of the patient; thus a daily quantity of 6 to 10 grms. indicates a good digestion, while less than 5 grms. shows an impaired nutrition.

Dr. Zuelzer has shown that under conditions of excitement of the system, the quantity of sodium chloride passed in the urine is diminished, while that of the potassium salt is increased; under conditions of depression the reverse obtains.

Sulphuric Acid, Sulphates, and other Sulphur Compounds.—Sulphuric acid is found in the urine as sulphates of potassium, sodium, and calcium, and these are obtained by concentration of the urine and crystallisation. The average amount of sulphuric acid discharged during the twenty-four hours amounts from 1·5 to 2·5 grms., the greater part occurring in the urine shortly after meals. Of course much of this sulphuric acid comes from the food, but another part is undoubtedly due to the oxidation within the system of the sulphur contained in some albuminous substances. That this is so, derives considerable support from the fact that there is also present in urine a small quantity of sulphur existing in such a form as to escape precipitation with salts of barium. It is not unlikely that this so-called unoxidised sulphur is directly derived from taurocholic acid or taurine. A great number of observations have been made regarding the quantity of sulphuric acid and sulphates found in the urine under various conditions of health and disease, but for the most part such observations are of little value for the present work and hence may be disregarded.

It would also appear that hyposulphurous acid, or sulphurous acid, or both, are sometimes contained in urine, since when such urine is treated with zinc and sulphuric acid a little sulphuretted hydrogen is set free. Thudichum has published a great number of determinations of the quantity of sulphur present in the urine in other forms than that of sulphuric acid, but it is unnecessary to do more than notice the fact.

Sulphuretted hydrogen has also been found in urine at various times, and particularly in cases of disease of the bladder. Moreover, another observer has also discovered what he believed to be hydrosulphocyanic ($HCNS$) in the urine, but no absolute proof of this statement of Gscheidlen has been forthcoming, and quite recently Thudichum has given denial to it.

Phosphoric Acid and Phosphates.—Considering how largely phosphate of calcium enters into the constitution of bones, and bearing in mind that large quantities of phosphorised principles occur in brain and nerve matter, &c., it is not surprising that the amount of phosphoric acid excreted in the urine should not merely be considerable, but that its determination often serves as a valuable guide in processes of disease.

Phosphoric acid exists in the body also in combination with various bases as orthophosphates.

It would appear from numerous researches that the average quantity of phosphoric acid discharged in the urine in twenty-four hours amounts from 1·2 to nearly 5 grms., but there is no doubt that the amount varies largely according to the nature of the food and other conditions. It should be remarked that this phosphoric acid occurs in the urine in combination with calcium, magnesium, potassium, and sodium.

Bases present in Urine.—Considerable information regarding the bases present in urine has been given under other headings, and a statement of the quantities so far as they have been determined is given in the table quoted from Thudichum's work in a previous section.

Other Matters occurring in Urine.

Trimethylamine is stated to be a constant ingredient of human urine, although it is present in mere traces. It has also been shown in other chapters that when sugar and alcohol are taken in large quantities traces of these substances occur in the urine. Among pathological ingredients are blood, albumin, fibrin, fatty acids and fats, sugar (as in diabetes), leucine, tyrosine, and certain colouring matters (as in cholera), and oxalic acid and oxalate of lime (as in certain diseases terminating in calculi).

Damalic and damaluric acids are of a volatile nature, and were discovered by Städeler[1] in the urine of a cow. It is doubtful whether they ever occur in human urine.

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[1] *Ann. Chem.* 77 (1851) 17.

Urinary Sediments and Calculi.

Under the general descriptions of urine, and uric acid as a constituent of urine, mention has been made to some extent of urinary sediments and calculi; and it will be sufficient here to supplement these observations by very few others.

Under healthy conditions the urine usually remains clear and transparent after micturition, but not infrequently it throws down certain deposits which may or may not indicate some sort of disturbance of the laws upon which health depends.

Sediments.—The sediments alluded to, are in some instances more or less flocculent, while at other times they are crystalline and generally coloured with principles about whose true nature we have but little information. Amorphous deposits occurring in acid urine generally consist of urates, sometimes associated with calcium phosphate and not rarely with fat globules; while when crystalline the deposits made from urine of an acid reaction consist of calcium oxalate, free uric acid, cystine, calcium phosphate, tyrosine, or hippuric acid, or a mixture of these bodies or some of them. At other times these deposits contain organised particles consisting of mucus, mucus and blood corpuscles, pus, casts of tubules, epithelial casts, granular renal casts, spermatozoa, or sarcina ventriculi, &c., or a mixture of a number of such bodies.

Again, when the urine is alkaline and the deposit crystalline, the latter may contain ammonio-magnesium phosphate, or urate of ammonium, or both; and when the sediment is amorphous, phosphate of calcium and organised particles.

Uric acid deposits do not dissolve when the urine is heated, and may be readily identified by the murexide and other reactions. The urates, however, dissolve on heating, and are insoluble in acetic acid but dissolve in alkaline solutions. These urates comprise the salts of sodium and ammonium, and more rarely urate of calcium.

The phosphates do not dissolve in alkaline solutions or when the urine is heated, but are readily soluble in acetic acid.

Calcic oxalate is not so commonly found in the sediments, but when present may be easily detected by its crystalline character and its chemical reactions.

Cystine ($C_3H_6NSO_2$) deposits in six-sided tables which dissolve in hydrochloric acid and ammonia, and may be recognised by the production of sulphide of lead when the acetate of that metal is added to a previously boiled alkaline solution of the deposit. Cystine is insoluble in water, alcohol, and ether, but is soluble in the stronger acids and in alkalies. It would appear to represent in some way the sulphurised nucleus of fibrin, &c.

Blood corpuscles are easily recognised under the microscope, while the spectroscope is a sure agent to employ in their detection.

Pus sediments are of a pale greenish colour, and in such case the urine generally contains albumin coagulable by heat and nitric acid.

Mucus (when present) is generally diffused through the urine as transparent flocculi.

Calculi.—The chief varieties of urinary calculi are as follows. Those containing or consisting of uric acid, ammonium and other urates, oxalate of calcium, phosphate of calcium, phosphate of ammonium and magnesium, xanthine, and cystine, all of which are generally constructed round a nucleus of some foreign substance such as blood corpuscles, &c. When the phosphate of calcium and the double salt of ammonium and magnesium occur together in calculi, these latter are known as 'fusible.' Important as a proper knowledge of calculi, and the conditions under which they appear, is to physicians, it would serve no useful purpose to enter into more minute considerations upon the subject in this place. Moreover, the nature and properties of urinary calculi have often been treated[1] in a complete way by able observers.

Other Morbid Conditions of the Urine.

In another chapter special consideration has been devoted to that disease—diabetes—in which the urine is charged with grape sugar. Under other conditions of disease (such as in albuminuria, Bright's disease, &c.) the urine is found to contain albumin in a state of solution. In such cases it is supposed that the seat of the evil is situated in the kidneys, their power of filtration and secretion being profoundly influenced. In cruenturesis, or intermittent hæmaturia, the urine contains or may contain hæmato-crystalline, calcium oxalate, hematine, &c., &c.

Again, in certain hepatic and other diseases, biliary pigments and fatty acids occur in the urine and may be detected by the ordinary tests.

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[1] See Golding Bird's treatise *On Urinary Deposits*; Beale's treatise *On Urine, Urinary Deposits, and Calculi*; Simon's *Chemistry*; Thudichum's *Pathology of the Urine*, &c., &c.

Unfortunately the exact steps by which these abnormal constituents of the urine are derived from the corresponding principles in the system, are almost entirely unknown.

Chylous urine is not often met with in Europe, and is peculiar through the circumstance that it contains certain constituents of the blood, or lymph, or chyle : notable among these is fibrin. The milky appearance presented by such urine is due to the suspension of fats and fatty acids.

Lactic acid has been observed in the urine by various chemists in cases of phosphorus poisoning, acute malignant jaundice, trichiniasis, and osteomalacia.

In typhus and variola; leucine and tyrosine—together with other products of a particular decomposition of albuminous principles—occur in human urine.

CHAPTER XIV.

SWEAT.

As is well known, man breathes, so to speak, not only through the mouth but also through the skin. In fact, the skin is an excretory organ, sweat being the excretion, or a part of it. The process is carried on through the agency of the sudoriparous glands which exist all over the surface of the body, and the watery fluid which is excreted passes off for the most part under ordinary conditions in the state of vapour, leaving, however, some part of the soluble constituents behind on the integument. Under these circumstances the process is termed insensible perspiration; but under the influence of active exercise, high external temperature, mental emotion, or diseased conditions, the secretion is elaborated in greater amount, and the process is then termed sensible perspiration, inasmuch as the sweat is deposited in the form of drops on the surface of the body.

The amount of sweat in health varies with a number of conditions, as for instance, the temperature and humidity of the atmosphere, the state of the blood and nervous system, &c. &c. Various attempts have been made to estimate the quantity, Seguin's observations being among the most valuable. He found that on the average about 1·2 grm. of fluid were discharged by the skin and lungs in one minute; of this quantity the skin exhaled 0·7 grm. and the lungs 0·5 grm. From a number of data he further concluded that the maximum amount of loss to the body during 24 hours by the agency of the skin and lungs averages about 5 lbs., and the minimum loss about 1 lb. Most of this loss consists of water, but there is some carbonic anhydride, perhaps a little nitrogen, and a yet smaller quantity of organic matters, to be considered more in detail hereafter.

As a general rule it is now considered that the quantity of water exhaled by the skin in a given time is about twice the amount passing off by the lungs, or about 2 lbs. in 24 hours. It is upon this evaporation of water from the surface of the body that the regulation of body temperature in no small measure depends. In the Chapters on Blood, Animal Heat, and Vital Force, we have studied the oxidation processes by which the blood is maintained at a high temperature, but its precision is chiefly regulated by the evaporation which takes place from the skin. In summer this evaporation takes place much more freely than in winter, for its extent depends not mainly upon the heat originating within the body, but rather upon the heat acting upon the body from without. Again, there is a nervous power which helps to regulate these processes. Cold produces an irritation of the walls of the blood-vessels, and causes them to contract; the first consequence is a reduced supply of blood to the surface, and as a further consequence, there is a less exudation from these vessels, for sweat is nothing more or less than such exuded liquid.

The amount of carbonic anhydride excreted by the skin is not more than $\frac{1}{30}$ or $\frac{1}{40}$ of that passing out by the lungs; but that it is regularly excreted may be shown by enclosing a limb of the body in a vessel containing air of known composition, and it will be found that in process of time the amount of carbonic anhydride increases as the quantity of oxygen decreases. Notwithstanding the undoubted change in composition of the blood effected by these processes going on in the skin, it is not converted from an arterial to a venous state.

The solid constituents of sweat are so small, and the secretion happens over such a large surface, that at present we have but little accurate knowledge of them.

In the normal state, the sweat contains free lactic acid and fatty matters, which are often increased in amount by admixture with the fatty products of the sebaceous glands. Moreover, as the sweat deposits in drops on the skin, it is associated with surface epithelium, the quantity of which increases with exercise and external temperature of body.

Simon and others have determined the specific gravity of sweat to be about 1003 to 1004. It contains from 0·5 to 1·25 per cent. of solid (not volatile) constituents. Among these constituents is urea, and Funke has estimated the quantity equal to about 0·7 grm. nitrogen during 24 hours.

Chloride of sodium is the most abundant constituent, while lactates, butyrates, and acetates of ammonium and sodium are also present, and attended with traces of calcic phosphate and ferric oxide. This latter substance is perhaps derived from the epithelium. Volatile fatty acids, such as valerianic and caproic acid are found sometimes, but it is doubtful whether they pre-exist in sweat or are formed from it during early changes which happen in it.

These changes seem to be due to the presence of a nitrogenous principle of unascertained composition.

Anselmino found [1] in 1000 parts of sweat—

Water	995·000	987·500
Epidermis and lime salts	·100	·250
Water extract and sulphates	1·050	2·625
Spirit extract, alkaline chlorides	2·400	6·000
Alcohol extract, acetates, lactates, &c.	1·450	3·625

In 100 parts of dried residue from sweat the same author found 22·9 of fixed salts, consisting of chloride of sodium, carbonates, sulphates, and phosphates of sodium and (in small quantity) of potassium, phosphate and carbonate of calcium, and traces of ferric oxide.

It is seen from the nature of the matters excreted in sweat that the actions of the lungs, kidneys, and skin are to a limited extent vicarious, and it so happens that serious interferences with the functions of the skin often lead to serious derangements of the lungs or kidneys.

Sweat in Disease.—Of morbid sweat we know yet less than of the normal secretion. In certain diseases, the amount of solid constituents is materially increased, and ammonium salts are particularly present.

In cases of intermittent fevers, rheumatic complaints, &c., critical sweats are usually abundant, continuous, and watery. In putrid fever and scurvy, the sweat has a putrid odour, and Nasse relates a case of diabetes in which sugar was found in the sweat.

Among other abnormal constituents of sweat the following are stated to have been observed: blood, uric acid, biliary colouring matters (as in jaundice), urinary colouring matters, much fatty matter, leucin, &c. &c.

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[1] Simon's *Animal Chemistry*. English edition, p. 105.

PART IV.

OTHER ORGANS, TISSUES, AND FLUIDS OF THE BODY

CHAPTER XV.

THE CHEMICAL CONSTITUTION OF THE BRAIN.

So voluminous is the literature of brain chemistry that, were it attempted to give anything like a complete history of the subject, it would amount to a treatise in itself. This, therefore, cannot be done here; and, indeed, it is unnecessary, for Thudichum has done it already as an appendix to his published researches on the brain, to which we shall more immediately devote our attention.

In justice, however, to other workers, we give a list of all authors, the dates of their publications, and, where necessary, the salient features in their work. For much of this matter I am indebted to Thudichum's papers already referred to:—

Name.	Date.	References to their Publications.
Hensing	1715	Examen chemic. Cerebri. Giessen, 1715.
Spielmann	1766	Mister. Chemiæ. Arg. 1766, p. 204.
Mönch Gurman Burrhus	—	See the notes of John to the translation of Vauquelin's research in Schweigger, 8 (1813) 431.
Thouret	1790	Journ. de Phys. 38 (1790) 329.
Fourcroy	1793	Ann. de Chim. 16 (1793) 282.
Vauquelin	1811	Ann. du Mus. d'Hist. Nat., 1811, p. 212–239; also in Ann. Chim. 81, 37. English translation in Ann. of Philos. 1332; German in Schweigger, 8 (1813) 430–460.

Name.	Date.	References to their Publications.
John	1814	Chemische Schriften, vol. 4, nro. 31, p. 228; and Zoo-chemische Tabellen, Tab. 1, A (1814), p. 12. Also Gilbert, Annal. 46 (1814) 329.
L. Gmelin	1826	Rep. f. d. Pharm. 52, 169; also Zeitschr. f. d. Physiol. von Tiedemann, und Treviranus, 1119; also in Gmelin and Tiedemann, die Verdauung nach Versuchen, 1826.
Kühn	1828	De Cholesterino eique similibus pinguedinis corporis humani formis. Diss. Lipsiæ, 1828. Abstracted in Kastner's Arch. f. Naturlehre, 13 (1828) 337.
Lassaigne	1830	Ann. Chim. 45, 215; also Journ. de Chim. Méd. 2nd series, 1, 344; Compt. Rend. 9, 703; 11, 763.
Couerbe	1834	Ann. Chim. 2nd series, 56, 160–193; see also Nouvelles Considérations sur le Cerveau. Compt. Rend. 10 (1840) 974.
Frémy	1841	Ann. Chim. 2, 463; also Journ. de Pharm. 27, 453; also Journ. de Pharm. et de Chim. 12 (1847) 13.
Gobley	1846, 1856, and 1875	Rech. Chimiques sur le Jaune d'Œuf. Journ. de Pharm. et de Chim. 9 (1846) 1, 81, 161; and Journ. de Pharm. et de Chim. 11 (1847) 409, and 12 (1847) 1. See also Bul. de l'Acad. de Méd. 15, 471; Journ. de Pharm. et de Chim. 17 (1850) 401, and 18 (1850) 107; also 19 (1851) 406; 21 (1852) 241; 30 (1856) 241. The 1875 paper is in J. de Pharm. et de Chim. (4) xx. 161–166.
Müller Liebig and Von Bibra are represented in	1857–1858	Ann. Chem. 103 (1857) 131. Ann. Chem. 105, 361 (1858).
Städeler and Frerichs	—	Verh. der Zürcher nat. Gesell. iv. 55, § 14.
Liebreich	1864	Ann. Chem. 134, 29.
H. Koehler	1867–1868	De Myelini quod vocant constitutione chemica disqu. Halae, 1867. See also Chem. Unters. über die fälschlich Honifelte genannten Substanzen und ihre Zersetzungsproducte. Halae, 1868.
Otto	1867	Chem. Centr. Bl. 12, 1022 (1867).
Diakonow	1867–1868	Cent. Bl. No. 1 (1868), and No. 7 (1868).

Name.	Date.	References to their Publications.
Strecker . .	1869	Sitz. Ber. d. Acad. d. W. München, 1869, 2, 269.
Baeyer . .	1868	Ann. Chem. 140, 306.
Klauss and Kessé	1867	Journ. pr. Chem. 102 (1867) 24.
D. Petrowsky .	1873	Pflüger's Archiv. vii. 254–263.
Thudichum .	1874	Reports of the Medical Officer of the Privy Council and Local Government Board. New Series, No. 3, 1874. Report. New Series, No. 8 (1876).
Thudichum and Kingzett	1876	Report. New Series, No. 8 (1876). Also Journ. Chem. Soc. July 1876; September 1876.
Kingzett . .	—	Chem. News, vol. xxxiv. p. 158; Pharm. Journ. February 26 and March 11, 1876; Pharm. Journ. June 9, 1877; Quarterly Journal of Science, January 1877.
R. v. Jaksch .	1877	Pflüger's Archiv. f. Physiologie, xiii. 469–474.
F. Selmi . .	1877	Gazzetta Chimica Italiana, vi. 468–471.

Hensing discovered the presence of phosphorus in the brain, and this constituted, perhaps, the first known fact relative to its composition.

Spielmann examined the ash of brain substance, and found in it particles of matter attracted by the magnet (iron or manganese).

Mönch obtained oxalic acid from brain matter by the action of nitric acid upon it (the oxalic acid was probably derived from cerebrin).

Gurman observed the prolonged conservation of the brains in the skulls of corpses.

Burrhus compared the brain to an oil mixed with spermaceti.

Thouret concluded that brain matter consisted of a soap, a fatty matter similar to, or identical with spermaceti, and a fixed alkali.

Fourcroy discovered the presence of an albuminous principle, a peculiar animal matter, and the phosphates of ammonium, sodium, and calcium. He subjected brain matter to the action of various reagents, and, by extracting it with alcohol, obtained yellowish-white plates, which were supposed to be analogous to spermaceti, but which were probably impure cholesterine.

Vauquelin's research was particularly brilliant in its results. He appears to have obtained a mixture of cerebrine with cholesterine, but did not succeed in separating them. He also obtained bodies of a fatty character (the phosphorised principles), but did not understand well what he had in his hands, although he proved the presence of phosphorus in organic combination. In fact, Vauquelin concluded that the phosphorus existed in a form like that in which it had been shown to be present in the roe of fishes by Fourcroy. Beyond the white phosphorised matter which received this partial examination in the hands of Vauquelin, another more oily substance was likewise obtained from the alcoholic mother liquors, and finally a water extract containing phosphates of calcium, magnesium, and potassium, osmazome (or soap-like extract), albumin, and sulphur. He estimated the quantities of these substances as follows :—

Water	80
White fatty matter	4·53
Red " "	0·70
Albumin	7·00
Osmazome	1·12
Phosphorus	1·50
Acid, salts, sulphur	5·15
	100·00

Vauquelin also made some observations regarding the putrefaction of brain substance, and found also that the nerves possessed a similar composition to the brain, but contained less fatty and more albuminous substance.

J. F. John, in an examination of the brain matter of calves, deer, chickens, and crayfish, repeated and confirmed many of the observations made by Vauquelin, but otherwise failed to advance, in any sense, the knowledge of brain chemistry.

L. Gmelin identified the cholesterine of the brain with that derived from gall-stones.

Kühn gave to one of the principles of the brain the name of cerebrine, and to another that of myelokon, but gave no absolute characteristics of either substance. He appears also to have first noticed the reddish-brown matter, afterwards described by Couerbe as céphalote.

Lassaigne gave the following analysis of the retina and the optic nerve:—

	Retina.		Optic nerve.
Water	92·90	Water	70·36
Saponifiable fat and cerebrin	0·85	Cerebrin	4·40
Albumin	6·25	Osmazome and salt	0·42
		Gelatine	2·75

Couerbe, in a comprehensive research, isolated the following principles of brain matter:—

A yellow pulverulent fat = Stéaroconote.
A yellow elastic fat = Céphalote.
A yellowish red oil = Eleéncéphol.
The white matter of Vauquelin = Cérébrote.
Cholesterine.

Unfortunately, by some accident, he was led to make the statement that the brain fats contained sulphur, and as this was afterwards discovered by Frémy to be erroneous, these researches were for a long time comparatively disregarded. Thudichum has, however, done full justice to Couerbe in his history of the literature of brain chemistry, and has shown how insignificant were the critical researches of Frémy in comparison with those of Couerbe.

Couerbe analysed his cérébrote with the following results:

C. . . . . = 67·878
H. . . . . = 11·100
N. . . . . = 3·399
S. . . . . = 2·138
P. . . . . = 2·332
O. . . . . = 13·213

Thudichum supposes that Couerbe unfortunately introduced his sulphur by the use of nitric acid containing sulphuric acid. The presence of phosphorus, as we now know, was also a proof of the impurity of the preparation; otherwise, the analysis altogether was a very fair one. Frémy assumed that the sulphur found by Couerbe was derived from admixture with albuminous matter; but this could not be, for not only are most albuminous matters insoluble in alcohol (the reagent employed by Couerbe), but even pure albumin contains less sulphur than was found present in the principles examined by Couerbe.

From the analysis given by the latter chemist of céphalote, it is seen that he did not obtain this principle (now termed kephaline), in anything like a pure state; nevertheless, he established its individuality. The same is true of his stéaroconote. The eleéncéphol described by Couerbe was probably a mixture of what is now termed lecithine, with its decomposition products and other impurities. The great credit due to Couerbe consists in the fact that he was the first chemist to submit the brain components to ultimate analysis, and in a day when the methods were not nearly so accurate as they have since become. He analysed cholesterine with correct results.

Frémy re-examined the cérébrote of Couerbe, and gave to it the name of cerebric acid; but he never obtained this substance free from phosphorus, which he said was often combined with sodium or phosphate of calcium. He also isolated what he supposed to be a new body, and named it oleophosphoric acid; he recognised that acids and other reagents readily caused the decomposition of this body into oleine and phosphoric acid, but failed to give an elementary analysis of his products. More recent researches have shown the error of Frémy's work; his oleophosphoric acid does not exist, but what he obtained was apparently a mixture of lecithine with its products of decomposition.

Frémy, however, described an improved method for the isolation of cholesterine, and noticed that in the process of putrefaction conducted upon brain matter, fatty acids are set free; but he was in error in supposing that these also exist to some extent naturally in the healthy brain matter. The observation of Frémy regarding brain putrefaction is comparable with a similar one made by Chevreul upon the fat of dead bodies, and another by Pelouze and Felix Boudet regarding palm oil; these observers found that a nitrogenous matter (probably of albuminous origin) splits up the fats into free fatty acids and glycerine. Chevreul had also already demonstrated in the blood the presence of fatty matter found also in the brain. (See the Chapter on Blood;

Thudichum and Kingzett's account of the phosphorised substance attached to the blood corpuscles.)

The first researches of Gobley, although conducted upon the yolks of eggs, had a very direct bearing upon brain chemistry. He found that they contain water, an albuminous body which he called vitelline, oleine, margarine, and a viscous substance. Lecanu had previously found cholesterine in the yolks of eggs, and Gobley submitted it to analysis and established its identity. On submitting the viscous matter to decomposition with acids and alkalies, he found that it was split up into oleic, margaric, and phosphoglyceric acid, and hence he supposed that these were originally present in combination with ammonia as a true soap. He also determined the presence of lactic acid, various mineral salts, and osmazome (or meat extract) in the yolks of egg.

Gobley's next research was conducted upon the brains of chickens, sheep, and men, and he obtained from these a viscous matter like that already described; but he withdrew his previously-announced view regarding this compound as a soap. Yet later, in researches upon the eggs of carp, he was led to assign the names of cerebrine and lecithine to those substances previously termed by Frémy cerebric and oleophosphoric acids, but he did not succeed (as we shall see hereafter) in fully establishing the nature of lecithine, which, together with some cerebrin, constituted his viscous matter. To the cerebrin from eggs he assigned the following composition :—

C.	66·85
H.	10·32
N.	2·29
P.	0·43
O.	19·61

The presence of phosphorus demonstrates that he did not obtain cerebrine in a perfectly pure state.

In another research, Gobley identified in the milt of carp the ingredients he had found present in eggs, and pronounced F. Boudet's seroline to be a mixture of oleine, margarine, cholesterine, and a little albumin. Finally, in his last work at this date, he maintained that the fatty acids obtained in the decomposition or putrefaction of bile are products of the splitting up of lecithine, although neutral fats and cholesterine are also normally present. Here Gobley relinquished his researches until quite recently, and it was left to Strecker to complete a research which had been attended with such pregnant and important results.

Liebig, in an essay on the extract of flesh, had raised the question whether the brain furnished products like to those obtained from muscular tissue, and in some preliminary experiments he subjected brain matter to the action of dilute baryta water, but failed to find kreatine among the products. Von Bibra studied also the water extract of brain matter, but failed to find kreatine, inosinic acid, inosite, and hypoxanthine; he determined the presence, however, of volatile organic acids, among them formic acid; he also showed the presence of lactic acid.

Bibra analysed a sample of impure cerebrin and failed to obtain metallic combinations of this principle. He pointed out the purple colour which this substance strikes with strong sulphuric acid, a matter which has been explained in the Chapter on 'Pettenkofer's reaction.' He also noticed the peculiar power possessed by cerebrin of swelling when placed in contact with water.

Müller imitated the process which Liebig had employed, but failed to obtain the two barium salts which that chemist had stated to be produced. He, however, found an albuminous body in the filtrate, and by suitable means identified the presence of cholesterine, sodium chloride, and kreatine when human brains had been employed. When ox brains were made the subject of study no kreatine was found, but a substance resembling leucine. In further experiments these observations were confirmed, and it was also shown that uric acid, a substance resembling xanthine or hypoxanthine, and inosite were among the extractives obtained by the baryta process.

Kreatin occurs only in small quantity in human brains, whilst Liebig found 36 grms. in 100 lbs. of lean horseflesh, 30 grms. in 86 lbs. of ox flesh, and 72 grms. in 100 lbs. of lean dog flesh. Müller only obtained half a grm. of kreatine from 24 lbs. of human brains. The presence of kreatine was confirmed by Lerch, of Prague.

Städeler and Frerichs found leucine in the brain, but Müller failed to find this or any homologue of it as a constituent. He obtained 12 grms. of calcium lactate from 50 lbs. of ox brains. Thudichum summarises Müller's results thus far as follows:—

(1) The brain of man, in the portion soluble in water, contains a small quantity of kreatine.

(2) On the other hand, kreatine is not present in ox brain, but the latter contains either leucine or a homologue.

(3) In both human and ox brain volatile acids of the [illegible] exist in very small quantities.

(4) Both human and ox brain contain considerable [illegible] lactic acid.

(5) Ox brain contains a little uric acid and some quantity of inosite.

(6) Succinic acid, glycogen, kreatinine, urea, cystine, and taurine could not be found in the brain.

In his next paper, Müller described his methods of isolating the principles of brain substance, and stated that cholesterine forms one-third of the constituents of the brain matter soluble in alcohol or ether. He also obtained cerebrine for the first time free from phosphorus, and gave to it the formula $C_{17}H_{33}NO_3$, based upon the composition:—

C.	68·35	68·56	—
H.	11·30	11·25	11·06
N.	4·69	4·53	4·29
O.	15·66	15·66	—

He submitted some of his preparation to the action of boiling nitric acid, and obtained an oily yellow body which solidified on cooling; this was recrystallised from alcohol and analysed with the following results:—

C. = 75·52
H. = 12·92
O. = 11·56

leading to the empirical formula $C_9H_{18}O$. As this substance was not (apparently) examined for nitrogen, no safe conclusion can be drawn from this experiment.

After some little work upon the phosphorised constituents, Müller thought it safest to consider the question as to the form in which the phosphorus is contained as unsettled.

O. Liebreich's research was almost confined to what he termed protagon, but what now appears to have been a mixture of various substances, including cerebrine and some phosphorised principles. When boiled with strong baryta water this mixture yielded glycerophosphoric acid, impure stearic acid, and a second seemingly new acid; also a new base which Liebreich termed neurine. The new acid was undoubtedly (as we now know) derived from the decomposition of the cerebrine group of substances.

Koehler recognised the presence of hypoxanthine and inosite in brain matter. He also analysed a phosphorised body in which the relation of nitrogen to phosphorus was as 1 : 1. He termed it myeloidine ($C_{40}H_{76}NPO_{10}$), but evidently it was not a pure individual, nor did his myeloidinic acid ($C_{74}H_{135}N_2PO_{25}$) present the necessary guarantees of a pure chemical individual. Koehler further described the properties of several other substances which he obtained, although in an impure condition. Thus the body which he named myelomargarine, and which he subjected to boiling with alcohol acidulated with sulphuric acid, was beyond doubt a decomposition product of cerebrine, produced by the very act intended to purify it (see Thudichum's researches); moreover it is probable that Koehler overlooked the presence of nitrogen in his product.

Otto also appears to have overlooked the presence of nitrogen in cerebrine, otherwise the results of his analyses were almost identical with those which Müller obtained when working with cerebrine similarly prepared. He studied somewhat the products of decomposition of this substance; for instance, those obtained by heating during twelve hours with hydrochloric acid. Among them he found a gelatinous matter resembling fat, and containing 71·2 per cent. C. and 12·2 per cent. H., and in the alchoholic mother liquor from its crystallisation a second body fusing at 66°, and containing 81·3 per cent. C. and 13·3 per cent. He further found a syrup which reduced copper solution, &c., and which contained 41·7 per cent. C., 6·7·32 per cent. H., but did not apparently identify it with glucose, which requires 40 per cent. C. and 6·66 per cent. H.

Otto's research might have been particularly valuable and fruitful in results had he not so persistently disregarded the presence of nitrogen in his substances, thus, for example, his method of decomposition would have yielded him the body termed psychosine by Thudichum.

Diakonow more particularly studied lecithine, and gave to it the formula $C_{44}H_{90}NPO_9 + Aq$. Its decomposition by boiling baryta water he represented as follows:—

$$\overset{\text{Glycerophosphoric Acid.}}{C_3H_9PO_6} + \overset{\text{Stearic Acid.}}{2(C_{18}H_{36}O_2)} + \overset{\text{Neurine.}}{C_5H_{15}NO_2} - 3H_2O = \overset{\text{Lecithine.}}{C_{44}H_{90}NPO_9}.$$

He found a substance answering to this description in the brain of cows, but he was so far wrong that lecithine from brain does not give two molecules of stearic acid, but one of stearic acid and one of oleic acid. Diakonow also studied the products of Koehler, and came to the conclusion that they were mixtures.

Strecker's first research was conducted upon eggs, but has a very direct bearing upon brain chemistry. He isolated the lecithine by precipitation from an alcoholic solution with an alcoholic solution of platinic chloride acidulated with hydrochloric acid. In other experiments he used cadmic chloride instead of the salt of platinum. Strecker found the platinum compound to be unstable in character, but admitting of purification by dissolving in ether and reprecipitating with alcohol. The cadmium compound is almost insoluble in ether, but soluble in acidulated alcohol. From the solutions of lecithine, the metals may be removed by sulphuretted hydrogen, and the filtrates, on treatment with a current of carbonic anhydride and evaporation, leave lecithine hydrochlorate as a waxy mass. From the solution of this, the HCl may be removed by oxide of silver, and the excess of this reagent by sulphuretted hydrogen.

Strecker gave to the platinum salt the formula $2(C_{42}H_{83}NPO_8)Cl_2PtCl_4$, and represented the decomposition of the free body with baryta water as follows:—

$$\begin{array}{ccccccccc} \text{Glycerophosphoric Acid.} & & \text{Choline.} & & \text{Oleic Acid.} & & \text{Margaric Acid.} & & \text{Lecithine.} \\ C_3H_9PO_6 & + & C_5H_{15}NO_2 & + & C_{18}H_{34}O_2 & + & C_{16}H_{32}O_2 - 3H_2O & = & C_{42}H_{84}NPO_9 \end{array}$$

It should be observed that he used the formula of palmitic acid, and gave to it the name margaric acid (which is really $C_{17}H_{34}O_2$, and which probably exists, and should therefore not be confounded with palmitic acid).

Baeyer repeated Liebreich's process and obtained neurine (choline), which he purified by precipitation of its hydrochloric acid solution with phosphowolframic acid, and decomposition of the compound with baryta water. The filtrate freed from baryta is yet coloured. He found the best method of purification to consist in making the platinic compound, and on examination of his different preparations he concluded that neurine is a mixture of two bases, giving the combinations

$$2(C_5H_{13}NO)2HClPtCl_4,$$

and

$$2(C_5H_{11}N)2HClPtCl_4;$$

and may contain a third base, giving the salt

$$2(C_5H_{13}N)2HClPtCl_4.$$

By heating a mixture of concentrated solution of the base obtained as described with concentrated hydriodic acid and phosphorus in a sealed tube to 120–150° C.

during some hours, Baeyer obtained large colourless prismatic crystals of the formula $(C_5H_{13}N)I_2$. This compound gave up to nitrate of silver or freshly precipitated chloride of silver only one iodine, and when chloride of silver was used one atom of chlorine was assimilated in its place, thus furnishing a substance which, when combined with platinic chloride, had the formula $2((C_5H_{13}N)ICl)PtCl_4$.

When digested in the warm with silver oxide, the iodide lost both iodines, and yielded a base which gave the salt $C_{10}H_{24}N_2O,2HCl,PtCl_4$; more probably

$$\left.\begin{array}{l}C_5H_{13}N\\C_5H_{11}(HO)N\end{array}\right\}2HClPtCl_4.$$

In connection with brain chemistry the important point in Baeyer's research is this: he was the first to show that brain matter furnishes the base $C_5H_{13}NO$. His other work showing the chemical relations of this substance is of subsidiary interest, at least for the moment. Incidentally it may be observed that A. W. Hoffmann obtained a substance of the composition $(C_5H_{13}N)Br_2$ by treating an aqueous or alcoholic solution of trimethylamine with ethylene-bromide; the product gave up to argentic nitrate one bromine, leaving a substance which (combined with platinic chloride) had the formula $2(C_5H_{13}N)Br_2Cl_2,PtCl_4$. Both bromines are removable by chloride of silver.

Von Babo and Huschbrunn[1] discovered a base named sinkaline as a decomposition product of sinapine (from mustard), and A. Clauss and C. Kesse claim to have established the identity of sinkaline with choline (meaning, probably, $C_5H_{15}NO_2$).

The further study of these bases will be continued in treating of Thudichum's and Kingzett's researches.

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[1] *Ann. Chem.* 84, 10.

D. Petrowsky in no way advanced the chemistry of brain substance, and, on the other hand, somewhat impeded its progress by asserting the presence of fats in the ether extracts. Brain matter contains no fats properly so-called. Petrowsky's other observations were in no way original. He, however, states that dried grey substance consists about half of albumin, a quarter of cholesterine and fats, and contains little cerebrine, its principal components being therefore albumin and water; while in the white matter cholesterine and fats form much more than half of the dried substance, albumin a quarter of the whole substance, and cerebrine is present in considerable amount.

Since the date of Thudichum's first researches on brain chemistry, M. Gobley has published the following table setting forth what he regards as the mean percentage composition of the brain:—

Water	80·00
Albumin (ordinary albumin, soluble in water)	1·00
Cephalin (an albuminoid matter insoluble in water)	7·00
Cholesterine	1·00
Cerebrine	3·00
Lecithine	5·50
Olein and margarin	traces
Inosite, creatine, xanthine, &c.	undetermined
Extractive matters (aqueous and alcoholic)	1·50
Chlorides of potassium and sodium	1.00
Phosphates of potassium, calcium, and magnesium	
	100·00

It will be seen from Thudichum's researches that this table is valueless because incorrect, but we give it out of respect to the great chemist who died soon after its publication.

R. v. Jaksch[1] discovered in the brain the substance termed by Miescher 'nuclein;' that is to say, he discovered an impure albuminoid, and as this discovery will receive critical notice in the Chapter on the Albuminous Principles, it may here be dismissed.

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[1] Pflüger's *Archiv. f. Physiologie*, xiii. 469–474.

F. Selmi,[1] from some experiments on the products of the putrefaction of brain matter, concludes that the brain in a putrefied state does not contain any of the lower acids of phosphorus, but a phosphorised compound of unknown nature. No doubt it may contain several compounds of unknown nature, produced by a re-arrangement of the products of decomposition of the original phosphorised and other components. The accuracy of F. Selmi's observations, however, we distrust, from the fact that he states phosphoric acid to have been obtained from a volatile product of putrefaction! This kind of research is not only unsatisfactory, but deserves no kind of commendation, or we should pause to notice a further paper by F. Selmi on 'An alkaloid obtained from the liver, the brain, and the wild poppy.' When the alkaloid has received an analysis the matter may, perhaps, be worth attention, but till then no statement regarding it should have been published.

In the foregoing pages a brief summary has been given of the researches antecedent to those of Thudichum and others which will be presented hereafter as representing the position of our knowledge to-day, and it is readily perceived, and must be acknowledged, that throughout the range of physiological chemistry, no subject can boast of so complete a literature or of a chemistry so well studied. It is therefore the more remarkable that in most, and even modern treatises on animal chemistry, the subject of brain chemistry is ordinarily sacrificed to the more complete descriptions of matters about which our real knowledge is relatively vastly inferior. For example, one well-known text book[1] out of 572 pages devotes little more than one page to the chemistry of the brain! In another book[2] the following analysis (?) is given of cerebral matter :—

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[1] *Gazzetta Chimica Italiana*, vi. 468–471.

Water	80
Fats	5
Albumin	7
Extractives and salts	8

In a third and even more modern treatise, by Prof. Karl B. Hofmann,[3] more space is devoted to 'nuclein'—an impure ordinary albuminoid—than to the whole brain chemistry, while eight pages are devoted to the structural formula of glycerine!

In contradistinction from such authors, we shall, in addition to what has been already described, now proceed to place the chemistry of the brain before the reader as it is known to us to-day. Before doing so, it may be stated that the publications of Thudichum (the references to which are given at the head of this chapter) form the chief basis of what will be presented. With these researches the author of this work had a personal connection so far as they have yet been published, holding at that time the post of chief professional assistant in the laboratory of which Dr. Thudichum was the head. Dr. Thudichum and the author also published several researches conjointly. The measure and manner in which these researches were conducted were such as can only be secured by the outlay of money in the power of Government alone to provide; and these conditions materially assisted of course towards securing lasting and great results. In fact it is not too much to say that, at no time in the history of this or any other country, has such an extended and fruitful research been conducted in the domain of physiological chemistry.

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[1] *Handbook for the Physiological Laboratory*, by Klein, Sanderson, Foster, and Brunton (Churchill, 1873).

[2] *Physiological Chemistry*, by C. H. Raffe.

[3] *Lehrbuch der Zoochemie*, von Karl B. Hofmann, Prof. der Phys. Chem. an der Universität Gratz (Wien, 1876).

Methods of Extraction of the Brain Principles; their Composition, Constitution, Properties, &c. &c.

The methods employed by the various workers whose researches have been summarised, consisted in processes of extraction by such solvents as ether, alcohol, water; the brain matter being variously prepared for such treatment by previous processes, such as coagulating the minced brain with reagents like baryta water or acetate of lead. Similar methods have been applied by Thudichum, and to a large extent they admit of variety, notably since we know better the properties and solubilities of the various principles which exist in brain substance. It will not be attempted, therefore, to fully describe all possible methods, but attention will be confined to the most direct and practicable modes of procedure. These proceedings will be better understood hereafter when studying the nature and properties of the various ingredients of brain matter.

The brain of man weighs from 3 to 4 lbs., while that of the ox weighs on the average 356 grms., or from 12 to 13 ounces, and has an average specific gravity of 1034 to 1035.[1] In Thudichum's researches a total of nearly 2000 ox brains were employed besides a large number of human brains. The white matter of human brain has a specific gravity of about 1041, while that of grey matter is about 1034.

Brain matter contains from 80 to 90 per cent. water, a fact on which Thudichum thus comments: 'This, in conjunction with the peculiar manner in which the water is contained, engenders a mobility of ultimate particles within certain limits of movement. It also gives penetrability by diffusion while excluding porosity and its capillary effects, by which means a ready nutrition by diffusion in one direction, and ready cleansing from the effete crystallisable products of life, are insured. Consequently the brain as a whole is essentially made up of colloid matter, and may be compared to a colloid septum, on the one side of which is arterial blood and cerebro-spinal fluid of the ventricles; on the other side, however, is cerebro-spinal fluid of the arachnoidal space and venous blood. It follows from this, that the large amount of water present in the brain is not there, so to say, mechanically, only like water in a sponge, but is chemically combined as colloid hydration water, or, better still, water of colloidation.'

The brains, after removal from the carcases, are first freed from the arachnoid and pia-mater by skinning, after which they are cleansed from clot and blood by a temporary submersion in water, as much as possible of which has afterwards to be removed by means of 85 per cent. alcohol. The alcohol is allowed to cover the brain matter, and is renewed from time to time, by which means the brain is hardened by dehydration, the alcoholic solution being kept, and ultimately yielding some part of the water extractives. The brain matter is next reduced to a pulp by means of a mincing machine, and is then worked into a paste with 85 per cent. alcohol on a fine hair sieve, through which it is gradually made to pass.

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[1] See 'Memoir on the Action of Alcohol on the Brain,' by C. T. Kingzett, *Chem. News*, vol. xxxiv. p. 159.

The pasty mixture thus obtained is next treated with more alcohol, and heated to about 50° C. for some time, and is then filtered through a cloth, the residual matter being extracted again and again to nearly perfection. The ultimate undissolved residue constitutes the albuminous part of the brain substance.

As the alcoholic extracts cool they deposit a white crystalline and granular precipitate, which Thudichum terms in his laboratory 'white matter.' After filtration from this substance, the mother liquors are concentrated by distillation, and on cooling again they deposit a semisolid viscous matter designated 'buttery matter.' By further concentration the mother liquors from this deposit yield a more limpid substance termed 'last oily,' but this has practically the same composition as the 'buttery matter,' and will be considered here as identical with it. The final filtrate, freed from alcohol, contains the rest of the watery extractives of brain substance. In this way the brain is split up into its albuminous framework; certain deposits containing its other immediate principles in admixture; and those constituents which are extracted by water. These principles comprise three classes of phosphorised and nitrogenous fats—the kephalines, myelines, and lecithine—together with cholesterine and a group of nitrogenous substances (cerebrines) partaking in part of the character of glucosides.

To separate and isolate these various principles a number of processes may be adopted, but the following one is preferable, as being applicable alike to the so-called 'white matter' and 'buttery matter,' which are identical otherwise than that they contain relatively different amounts of the several principles.

They are first of all extracted with ether, which furnishes a reddish-coloured solution of a fluorescent character, and leaves an insoluble white pulverulent mass consisting mainly of the cerebrines and myelines, which may be separated to some extent by fractional recrystallisation from hot alcoholic solutions, or by fractional precipitation from alcohol with such solutions as alcoholic lead acetate and cadmic chloride. The ether solution contains the kephalines, together with cholesterine, lecithine, and some smaller quantities of the other principles rendered soluble by means of those here mentioned.

By treating the ethereal solution with an equal volume of absolute alcohol, the kephalines are precipitated in a comparatively pure condition; to render them quite pure, processes are applied which will be described hereafter.

The mother liquor after the kephalines, is distilled to rid it of the ether and some of the alcohol, and on cooling it deposits a great part of the cholesterine; if the distillation be carried further, lecithine is thrown down as an oily body admixed with some cholesterine, and remains in solution when the deposit is recrystallised from alcohol. It may be precipitated out of the solution by an alcoholic solution of cadmic chloride, a method which may be applied to the alcoholic mother liquor in which the deposition of lecithine has been intentionally avoided. The cadmic chloride salt thus obtained, is not pure; it contains some kephaline salt (which may be extracted by ether) and a little myeline salt, which is more difficult to remove. The solution resulting after the separation of the cadmic chloride precipitate by filtration, yields a further quantity of cholesterine when it is distilled to a lower bulk.

When the operator is sufficiently acquainted with the characters of these various substances, it is possible to vary very considerably the methods of separation, more especially when it is desired to isolate only one particular principle. Some of these methods will be described in the several sections treating of the individual principles of brain matter.

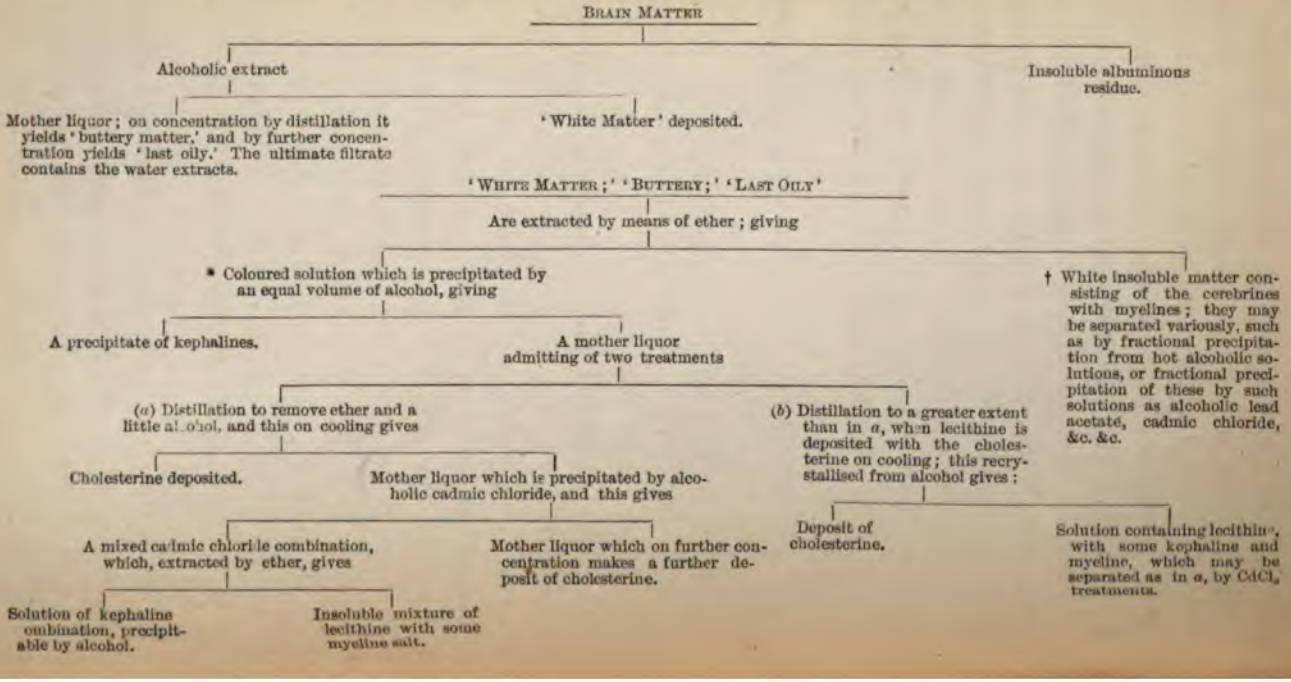
The process above described is represented diagrammatically on the next page.

Another process for the separation of the principles contained in 'white matter,' 'buttery matter,' and 'oily matter,' is as follows:—

They are extracted with cold absolute alcohol, with the view of dissolving as much lecithine with as little admixture as possible, and the alcoholic extract exposed to a freezing mixture, by which means some myeline is deposited, after which it is concentrated by distillation to remove by deposition on cooling, as much kephaline as possible (with myeline), and is then precipitated with alcoholic platinic chloride, and the voluminous yellow precipitate extracted with ether. What dissolves is mainly lecithine platinum salt, while some myeline salt remains undissolved.

The matter left undissolved by the cold alcohol is extracted by ether, which removes the kephalines, cholesterine, and some myeline, and leaves insoluble the cerebrines with some myeline. These latter may be

The brains are skinned, washed, hardened in alcohol, minced, worked through a sieve with alcohol, and extracted therewith at 50° C., filtered, and filtrate allowed to cool.



BRAIN MATTER

- Alcoholic extract
  - Mother liquor; on concentration by distillation it yields 'buttery matter,' and by further concentration yields 'last oily.' The ultimate filtrate contains the water extracts.
  - 'White Matter' deposited.
- Insoluble albuminous residue.

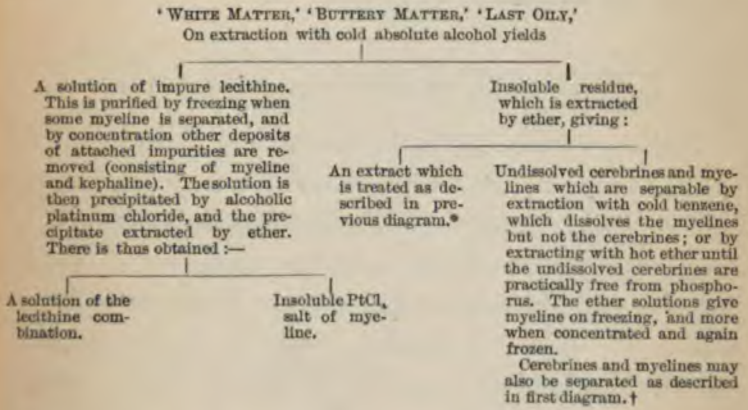
'WHITE MATTER;' 'BUTTERY;' 'LAST OILY'

Are extracted by means of ether; giving

- * Coloured solution which is precipitated by an equal volume of alcohol, giving
  - A precipitate of kephalines.
  - A mother liquor admitting of two treatments
    - (*a*) Distillation to remove ether and a little alcohol, and this on cooling gives
      - Cholesterine deposited.
      - Mother liquor which is precipitated by alcoholic cadmic chloride, and this gives
        - A mixed cadmic chloride combination, which, extracted by ether, gives
          - Solution of kephaline combination, precipitable by alcohol.
          - Insoluble mixture of lecithine with some myeline salt.
        - Mother liquor which on further concentration makes a further deposit of cholesterine.
    - (*b*) Distillation to a greater extent than in *a*, when lecithine is deposited with the cholesterine on cooling; this recrystallised from alcohol gives:
      - Deposit of cholesterine.
      - Solution containing lecithine, with some kephaline and myeline, which may be separated as in *a*, by $CdCl_2$ treatments.
- † White insoluble matter consisting of the cerebrines with myelines; they may be separated variously, such as by fractional precipitation from hot alcoholic solutions, or fractional precipitation of these by such solutions as alcoholic lead acetate, cadmic chloride, &c. &c.

separated by extraction with cold benzene, in which the cerebrines are insoluble, or by extraction with hot ether until the residual matter (cerebrines) is free from phosphorus. From the ethereal solutions on cooling (aided by freezing mixture) the myelines are deposited, and what remains in solution is obtained on distillation. The kephaline solution is treated as described in the first method previously sketched.

This process, sketched diagrammatically, may be thus represented :—



'WHITE MATTER,' 'BUTTERY MATTER,' 'LAST OILY,'
On extraction with cold absolute alcohol yields

A solution of impure lecithine. This is purified by freezing when some myeline is separated, and by concentration other deposits of attached impurities are removed (consisting of myeline and kephaline). The solution is then precipitated by alcoholic platinum chloride, and the precipitate extracted by ether. There is thus obtained :—

A solution of the lecithine combination.

Insoluble $PtCl_4$ salt of myeline.

Insoluble residue, which is extracted by ether, giving :

An extract which is treated as described in previous diagram.*

Undissolved cerebrines and myelines which are separable by extraction with cold benzene, which dissolves the myelines but not the cerebrines; or by extracting with hot ether until the undissolved cerebrines are practically free from phosphorus. The ether solutions give myeline on freezing, and more when concentrated and again frozen.

Cerebrines and myelines may also be separated as described in first diagram.†

The 'white matter' contains, as the predominating constituents; cerebrines, the myelines, and cholesterine; the other matters are also contained. In the 'buttery matter' the predominating principles are the kephalines; but again the other matters are present in more or less amount; while in the 'last oily,' lecithine is the most abundant constituent.

As already explained, these terms, 'myelines,' 'kephalines,' 'cerebrines,' &c., have reference to a number of well-defined substances, presented in groups, but comprising members of individual characteristics. The description of them which will be given presently will throw much light upon the various methods by which they admit of isolation and separation from each other.

It is proposed, first, to study group by group, and member after member, until the whole of them shall have been described, including those bodies which, in their conjoint existence, constitute the 'watery extractives' of brain matter; this done, it will be easy to pass on to general chemical considerations affecting the brain as a whole, in health or disease.

The Albuminoid Principles of the Brain.

These require but little description, because, so far as they have at present been studied, they present but little difference from the albuminous constituents of the body in general. They seem to comprise a certain quantity of soluble albumin, but the great mass is insoluble in water; it is also insoluble in the various solvents which have been described while sketching the manner in which the various principles may be isolated.

The Phosphorised Principles.

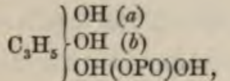
This group includes kephaline, myeline, and lecithine, and any varieties of these substances.

They all dissolve in water 'in a certain manner and measure' (Thudichum). Kephaline appears to be the most soluble, and myelin the least soluble.

Kephaline dissolves in ether as readily as butter, and lecithine almost as easily; the solubility of myeline in ether is not great.

On the other hand, myeline is readily soluble in hot alcohol, and kephaline not nearly so soluble; lecithine is even more soluble, both in hot and cold alcohol, than myeline.

All these principles contain carbon, hydrogen, nitrogen, phosphorus, and oxygen, and all may be regarded as built upon a common type. They differ only in certain subsidiary radicles, and may be represented as glycerophosphoric acid:—



$$C_3H_5\left\{\begin{matrix}OH\ (a)\\ OH\ (b)\\ OH(OPO)OH,\end{matrix}\right.$$

or $C_3H_9PO_6$, in which the two hydroxyls (*a* and *b*) are substituted by the residues of fatty acids, while one of the hydroxyls of the phosphoryl is substituted by an ammonium base.[1]

The glycerophosphoric acid being itself a derivative of glycerine, it will readily be perceived that these phosphorised principles possess a wide range of chemical affinities; thus, in a certain manner they are fats, and exhibit certain soapy characters; they are also acids, and at the same time they are bases; while, again, certain properties assimilate them to the alkaloids. Thudichum and Kingzett have shown that the glycerophosphoric acid yielded by all of them is one and the same substance; the same is true of the ammonium base; it is therefore only in the nature of the fatty acid radicles that they differ one from the other in their simplest forms—that is, when they may be viewed as being derived from an unitary molecule of glycerine. The more complex compounds seem to be derived from conjugated molecules of glycerophosphoric acid, and hence, while their general structure remains constant, wider differences are presented in individualities.

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[1] On *Glycerophosphoric Acid and its Salts, &c.*, by Thudichum and Kingzett; *J. Chem. Soc.* July 1876.

As these phosphorised principles exist in brain matter, and as isolated therefrom, they are associated with certain salts by a power of combination derived, as already explained, from their alkaloidal nature. To obtain these salts or bases it is only necessary to dissolve the compounds in water, and to precipitate the organic principles by dilute hydrochloric acid. The hydrochloric acid solution, on examination, is found to contain calcium, magnesium, and phosphoric acid in quantity, as well as potassium, sodium, and ammonium, while traces of iron and copper are also generally present.

Commenting on kephaline, Thudichum speaks of it as remarkably oxidisable; but this is a property by no means thoroughly made out; whatever tendency it may exhibit to undergo oxidation must reside in the nucleus of which we shall have more to say hereafter—the fatty acid containing about 26 (?) atoms of carbon; the other nuclei cannot be said to be oxidisable centres.

While myelines are particularly stable bodies, lecithine is equally as unstable, and splits up most readily into its proximate nuclei.

All the phosphorised principles of brain matter give with strong sulphuric acid and sugar the violet reaction described in another chapter as 'Pettenkofer's reaction.'

Kephaline ($C_{42}H_{79}NPO_{13}$),

may be purified to some extent by its repeated solution in ether and reprecipitation by absolute alcohol, but this method does not furnish it free from inorganic principles with which it appears to exist, at least partly, in combination in the natural state. Of this combinative power we shall have more to say presently. To rid kephaline of these matters, it is best to dissolve it in water (10 grms. to the litre) and after deposition of any insoluble matter, to filter the emulsive solution and precipitate it with hydrochloric acid. In this way an insoluble hydrochlorate is produced, which admits of washing to some extent; if washed with a great excess of water the hydrochloric acid is removed from combination and the free kephaline again dissolves in the water. This re-solution is indicated by a preliminary swelling of the substance, and when this happens the kephaline should be taken up once more with ether and reprecipitated with alcohol. In this way it may be obtained perfectly pure, and then presents a composition represented by the formula $C_{42}H_{79}NPO_{13}$.

Kephaline, when recently precipitated, dissolves slowly in cold absolute alcohol (about 7 grms. to the 120 c.c.), and somewhat more freely in boiling alcohol. In ether it dissolves to almost any extent, and the reddish-coloured solution shows a powerful green fluorescence; it is also soluble in benzene. Its aqueous solution is precipitable by almost every reagent, including acids, bases, and salts, but by washing with much water these latter may be almost entirely removed, when the kephaline begins to swell and afterwards dissolves.

Kephaline itself is a colloid, and thus it admits of partial purification by dialysis.

When its ethereal or alcoholo-ethereal solution is precipitated with an alcoholic solution of cadmic chloride or acetate of lead, the bodies so obtained are not definite in composition; that is to say, neither the cadmic chloride or lead are present molecule for molecule with the kephaline, but are variable in amount. These salts are also soluble in ether and reprecipitable by alcohol.

When the cadmium salt in ethereal solution is treated with sulphuretted hydrogen, no precipitation occurs, but a yellow solution is formed from which a new class of mercaptan-like bodies may be isolated.

When an aqueous solution is precipitated by a solution of platinic chloride acidified with hydrochloric acid, the light flocculent matter thus obtained is of a yellow colour, and contains these substances in combination in the relative proportions expressed by $2HCl,PtCl_4$, but the two together bear no definite relation to the molecule of kephaline, and for the reason already stated, namely, that the water of the reagents employed is sufficient to partly or entirely remove the precipitants.

By boiling with strong alkalies, such as soda, potash, and baryta water, kephaline is decomposed, yielding the barium salts of certain fatty acids insoluble in water, and an alkaline solution containing glycerophosphoric acid and an ammonium base which is liable to partial decomposition, yielding trimethylamine. Boiling with acids effects a similar decomposition although more slowly.

When baryta is employed, the salts of the fatty acids thus obtained may be separated to some extent by ether, which dissolves a dark coloured brownish red salt and leaves an almost white salt behind. This insoluble salt appears to consist of crude stearate of barium, but the composition of the soluble one has not yet been clearly made out. The acid is, however, apparently related to certain biliary substances.

From the baryta solution the glycerophosphoric acid may be extracted by various methods, one of the best of which consists in precipitation with a salt of lead, suspension of the lead salt in water, and decomposition with hydrosulphuric acid. The mother liquor, after the glycerophosphate of lead, yet contains the ammonium base which may be obtained after removal of the excess of lead, by concentration, neutralisation with hydrochloric acid, and precipitation with alcoholic platinic chloride. Or it may be isolated from the solution by means of Sonnenschein's method, employing phosphomolybdate of sodium, decomposition of the precipitate thus obtained with baryta, conversion into hydrochlorate, and precipitation as platinum salt.

After recrystallisation from water the platinum salt presents a composition exactly represented by the formula $2(C_5H_{13}NO)2HCl,PtCl_4$; at least this constitutes the main product. Two other bases, probably derived from this one, are sometimes obtained, and these will be described later on.

By the addition of the substances :—

Stearic acid	$C_{18}H_{36}O_2$
Glycerophosphoric acid	$C_3H_9PO_6$
Base	$C_5H_{13}NO$
We obtain	$C_{26}H_{53}NPO_9$.

Hence, without taking into consideration the water assimilated in the decomposition which furnishes these products, it appears that the acid whose nature has yet to be ascertained contains 16 atoms of carbon to the molecule (?). If not, then the formula of kephaline would have to be doubled or otherwise increased.

The composition of kephaline may, therefore, for the time, be regarded as follows:—

$$C_3H_5\begin{cases}\text{Fatty acid radicle } (a) = C_{18}H_{35}O_2 \\ \quad ,, \qquad ,, \qquad ,, \quad (b) = \text{undetermined} \\ HO(OPO)C_5H_{13}NO.\end{cases}$$

Thudichum has given analyses which in his opinion support the idea of the existence of bodies belonging to the kephaline class, of the formulæ $C_{43}H_{79}NPO_{14}$ and $C_{42}H_{79}NPO_{15}$; also amido-kephalin, $C_{42}H_{80}N_2PO_{13}$, but our personal association with these substances, supplemented by more recent knowledge, does not lead us to accept the theory of Thudichum. At any rate, before their existence can be accepted without doubt, more decided proofs must be forthcoming than have yet been furnished.

Thudichum assigns the name 'kephaline' to that principle furnished by the crude product termed 'white matter,' while to that furnished by 'buttery matter' he gives the name 'kephaloidine'; they are, however, identical in composition, and only differ in certain physical characters, probably depending upon the presence of associated substances, &c.

The Myelines.

The name 'myelines' is given by Thudichum to a number of allied principles distinguishable from kephaline and lecithine, as already pointed out in describing the methods employed to separate these various substances.

They must not be confounded with the substance described by Virchow, which was necessarily a mixture of various substances.

The myelines crystallise from alcohol in needles and granules, which remain white and powdery on drying, but under other conditions they exhibit a tendency, while drying, to cake into a hard waxy transparent state.

The myelines dissolve in water after the manner of kephaline, but not to so large an extent.

The alcoholic solutions are precipitable by such salts as acetate of lead, platinic chloride, and cadmic chloride.

The ethereal solutions deposit part of the matter held dissolved, when subjected to a process of freezing.

The cadmic chloride combination swells when placed in water, and is broken up, the cadmic chloride passing into solution; it is soluble, moreover, in boiling alcohol, but insoluble in ether.

The mixed platinum salts admit of some kind of separation by boiling with alcohol, when a part dissolves and is reprecipitated on cooling, while another part remains undissolved.

When the platinum and lead salts are suspended in hot alcohol and subjected to a current of sulphuretted hydrogen, the metals are precipitated as sulphides, and the free principle is dissolved by the hot alcohol which deposits myeline after filtration and subsequent cooling.

By virtue of their relative insolubility in cold ether, the myelines admit of ready separation from kephaline, and lecithine may be removed from it by cold absolute alcohol, after which they may be purified by any of the methods heretofore described. The cerebrines being almost insoluble in boiling ether, the myelines may be isolated from such admixture by taking advantage of this circumstance.

Various so-called myelines, having general properties in common, have been described by Thudichum; these include bodies represented by the empiric formulæ, $C_{40}H_{85}NPO_8$; $C_{40}H_{75}NPO_{10}$; $C_{40}H_{82}N_2PO_{10}$; $C_{52}H_{106}N_2PO_9$;

$C_{39}H_{81}NPO_8$; $C_{39}H_{82}N_2PO_8$; and among the compounds of these principles are salts of lead, such as $C_{40}H_{73}PbNPO_{10}$, also of platinum and cadmic chloride.

Many of these formulæ are derived by calculation from larger molecules; for instance, the substance $C_{120}H_{251}N_5P_3O_{24}$ is represented by Thudichum as—

$$\left.\begin{array}{l} C_{40}H_{81}N_2PO_8 \\ C_{40}H_{83}NPO_8 \\ C_{40}H_{81}N_2PO_8 \end{array}\right\}$$

Again, we have the compound $C_{84}H_{165}N_3P_2O_{18} + 2CdCl_2$ represented as

$$\left.\begin{array}{l} C_{42}H_{83}NPO_9CdCl_2 \\ C_{42}H_{82}N_2PO_9CdCl_2 \end{array}\right\}$$

But without multiplying formulæ to any unnecessary extent, it will be best to study the decomposition of some of these principles, and as the last named one has been most particularly investigated, our attention may be confined to it.

In this way a general insight into the composition and constitution of these substances will be afforded.

Before doing this, however, we may call attention once more to the discovery of Thudichum and Kingzett of one of the myeline principles present in blood corpuscles, whose composition was shown to be identical with one of the brain components. (See Chapter on the 'Chemistry of the Blood.')

The body of the composition $C_{84}H_{165}N_3P_2O_{18}2CdCl_2$ is one obtained direct in the processes of extraction of brain matter above sketched. It may be freed from cadmic chloride by standing in contact with renewed quantities of water, when it swells greatly and yields the whole of this salt to the water. On boiling the product with baryta water in an open dish, it was split up into palmitic acid ($C_{16}H_{32}O_2$); a new acid whose barium and lead salts were soluble in ether (perhaps of the composition $C_{26}H_{48}O_4$), glycerophosphoric acid, and the base $C_5H_{13}NO$; several other products were simultaneously obtained, the principal one being represented by the formula $C_{55}H_{113}NPO_7$. This was subjected to further chemolysis[1] with baryta water in a sealed tube at 130° C., and yielded more palmitic acid ($C_{16}H_{32}O_2$) and the body $C_{39}H_{86}NPO_8$, as the only products, thus :—

$$C_{55}H_{113}NPO_7 + 3H_2O = C_{39}H_{86}NPO_8 + C_{16}H_{32}O_2.$$

In recapitulation of these results it may be said that under the name of myelines Thudichum includes a number of substances which appear to have the same general structure as that above assigned to kephaline; that is to say, those included in this description yield glycerophosphoric acid, and the base $C_5H_{13}NO$; they also yield palmitic acid, by which they are characterised, and a new acid having somewhere about 26 atoms of carbon.

It also appears that certain molecular combinations exist which are not so readily broken up by processes of hydration, and among these the body $C_{39}H_{86}NPO_8$ is prominent. It is impossible to say yet in what state the nitrogen of this substance exists.

In brief, these processes of decomposition require much more study before final and definite statements may be made and accepted.

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[1] Thudichum uses the word 'chemolysis' to indicate the direct decomposition of bodies into their proximate nuclei.

Brain Lecithine.

The platinum chloride combination of lecithine is, when recently prepared, soluble in ether, but if kept for any time in the air or in the vacuum, it decomposes, oleic acid being set free in oily drops; the residual platinum salt is then insoluble in ether.

When the platinum salt is boiled with hydrating agents such as baryta water, it is decomposed, yielding glycerophosphoric acid, the base $C_5H_{13}NO$, apparently margaric acid, $C_{17}H_{34}O_2$, and oleic acid, $C_{18}H_{34}O_2$. From these results a constitution may be assigned to brain lecithine as follows :—

$$C_3H_5 \begin{cases} C_{18}H_{33}O_2 \\ C_{17}H_{33}O_2 \\ OH(OPO)C_5H_{13}NO\text{; or a total of } C_{43}H_{84}NPO_8. \end{cases}$$

Strecker assigned the formula $C_{42}H_{84}NPO_9$ to egg lecithine, and, excepting that he obtained palmitic in the place of margaric acid, and a base which he regarded as $C_5H_{15}NO_2$ instead of $C_5H_{13}NO$, this substance is identical with that obtained from brain matter.

It will be shown hereafter that Strecker was probably in error in assigning the given formula to the ammonium base, and further researches are required before it can be absolutely decided whether the second fatty acid is palmitic, margaric, or stearic acid; the first one is undoubtedly oleic acid.

The general characters of lecithine are similar to those of myeline and kephaline, but certain broad distinctions are visible; these have been sufficiently pointed out in treating of the other phosphorised principles and while describing the methods employed to isolate them.

Glycerophosphoric Acid and its Salts.[1]

Glycerophosphoric acid was first synthetically prepared by Pélouze by heating glycerine and phosphoric acid together at an elevated temperature. Gobley shortly afterwards obtained it from egg lecithine, and subsequently Lehmann observed its presence in diseased brain matter. Thudichum and Kingzett's observations regarding glycerophosphoric acid were made upon that which results from the decomposition of the phosphorised brain principles which have just been studied. They describe the normal lead, $C_3H_7PbPO_6$; the normal calcic salt, $C_3H_7CaPO_6$; further, what is probably an acid calcium salt, of the formula $C_3H_7CaPO_6,C_3H_9PO_6$; also the barium salt, $C_3H_7BaPO_6$, and a hydrate of this, $C_3H_7BaPO_6H_2O$. What is more curious is the body which the authors describe as an alcoholo-hydrated barium glycerophosphate, that is to say, a body which is at once a hydrate and contains alcohol in place of some water of crystallisation; it may be $C_3H_7BaPO_6,6H_2O,3C_2H_6O$.

The most characteristic salt is that of calcium, which being less soluble in the hot than in the cold, is consequently deposited when its saturated solution is heated to boiling. The barium salt shares this property to some extent. The free acid is somewhat unstable, and is by the prolonged action of alkalies in excess, split up into glycerine and phosphoric acid; hence it results that when the brain principles are decomposed by baryta water, the theoretical amount of the acid is not obtained, more or less being decomposed into the afore-named substances.

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[1] On *Glycerophosphoric Acid and its Salts, as obtained from the Phosphorised Constituents of the Brain.* J. L. W. Thudichum and C. T. Kingzett; *Journ. Chem. Soc.* July 1876.

Neurine and Allied Bases.

It has already been shown that Liebreich obtained from the brain a base soluble in alcohol, but which he did not examine in detail. Diakonow afterwards gave to it the formula $C_5H_{15}NO_2$, and called it neurine or trimethyl-oxaethylammonium hydroxide. The body which Strecker obtained[1] from egg-yolk was considered by him identical with this substance, and also with choline derived from bile (see Chapter on the 'Chemistry of Bile'). He did not, however, subject his preparation to complete analysis, but only estimated the platinum and the chlorine. The base obtained in Thudichum's researches upon brain matter is evidently the same substance and whose hydrochloride platinic chloride combination presents a composition invariably represented by the formula $2(C_5H_{13}NO)2HCl,PtCl_4$; at the same time it may be observed that different crystalline forms of this compound are obtainable, even while the composition appears to be uniform.

Thudichum, writing of this compound, says,[2] 'The formula of $C_5H_{15}NO_2$ is rather presumed than proved as regards the exact quantity of hydrogen and oxygen, for if the HCl were like the $PtCl_4$, merely an addition, then the formula of the free base would be $C_5H_{13}NO$; but if the chloride were a product by substitution of hydroxyl by Cl, and expulsion of the hydroxyl as H_2O, then the larger formula for the free body would be correct.'

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[1] Strecker, *Ueber das Lecythin*, 1868.

[2] *Rep. Med. Off.* New Series, No. viii. p. 127.

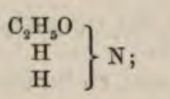
In some critical notes[1] on these bases I have objected to this view of Thudichum, and maintain that the free base when derived from brain matter has undoubtedly the formula $C_5H_{13}NO$; of the substitution which Thudichum seems inclined to favour there is no evidence whatever. It is quite possible that a hydrate, $C_5H_{13}NO,H_2O$, may exist. Thudichum also obtained two secondary bases evidently derived by a decomposition of the primary one ($C_5H_{13}NO$), and their platinic combinations had the formulæ

$$(a)\ 2(C_2H_7NO)2HCl,PtCl_4$$

and

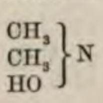
$$(b)\ C_5H_{14}N_2O,HCl,PtCl_4$$

The first of these may, perhaps, be regarded as oxethylamine—



$$\left.\begin{matrix} C_2H_5O \\ H \\ H \end{matrix}\right\} N;$$

or as dimethylamine hydroxide—



$$\left.\begin{matrix} CH_3 \\ CH_3 \\ HO \end{matrix}\right\} N$$

The relation of the second base to the two others is not so clearly perceptible.

In giving a sketch of the literature relating to brain chemistry, we have already alluded to the labours of Baeyer, who also obtained the compound $2(C_5H_{13}NO)$ $2HCl,PtCl_4$ among others; his results were supported and confirmed by those of A. W. Hofmann and Wurtz.

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[1] *Pharm. Journ.* and *Trans.* June 9, 1877.

Harnack[1] has found in the red fungus which yields muscarine (said to be isomeric with betaine) another alkaloid which he terms amanitine and regards as $C_5H_{15}NO_2$.

$$N \left\{ \begin{array}{l} (CH_3)_3 \\ CHOH-CH_3 \\ OH. \end{array} \right.$$

In another paper[2] Schmiedeberg and Harnack state that choline or neurine, sinkaline, and synthetically prepared hydrox-ethylentrimethyl-ammonium are identical, and all yield muscarine upon oxidation. To this latter substance they assign the formula $C_5H_{13}NO_2$; or

$$N \left\{ \begin{array}{l} (CH_3)_3 \\ CHOH-CH \\ OH, \end{array} \right.$$

and state that it forms the compounds

$$C_5H_{13}NO_2,2HCl,PtCl_4 + 2H_2O,$$

and

$$C_5H_{13}NO_2,HCl,PtCl_4.$$

Muscarine is hence said to be identical with betaine, and yields with silver oxide the hydroxide $C_5H_{15}NO_3$.

$$N \left\{ \begin{array}{l} (CH_3)_3 \\ C_2H_5O_2 \\ OH. \end{array} \right.$$

The oxidation of choline and its so-called isomers into muscarine is not effected, according to Schmiedeberg and Harnack, by means of the milder oxidants such as potassic permanganate or chromic acid, but requires strong nitric acid and evaporation therewith to dryness! This is the more remarkable since the only empirical difference presented by amanitine and muscarine is H_2. Thus,

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[1] *Chem. Centr.* 1875, 629–630.

[2] *Archiv. für Experimentelle Pathologie u. Pharmakologie*, vol. vi. p. 101.

Amanitine . . . . = $C_5H_{15}NO_2$
Muscarine . . . . = $C_5H_{13}NO_2$.

Besides therefore the improbability attached to the formula which the authors in question use for choline, this remarkable fact regarding oxidation and other considerations causes considerable doubt to be attached to the conclusions of Harnack and Schmiedeberg.

It should be remembered that betaine has been constructed synthetically by Peter Griess,[1] who regards it as trimethylglycocine, $C_2H_2(CH_3)_3NO_2$, or $C_5H_{11}NO_2$. He obtained it by acting upon glycocine in alkaline solution with methyl iodide, and although it may be identical with the betaine obtained from beet-root by Scheibleis, it is certainly distinct from the base derivable from brain matter.

Moreover, it must be borne in mind that there are a whole series of so-called betaines or trebly-substituted amido-acids, those *par excellence* being trimethyl and triethyl glycocine (see paper by J. W. Bruhl[2]). This fact, and the futility of the methods of analysis at present known to explain isomerism, should make us particularly careful in drawing conclusions regarding the identity or constitution of bodies so nearly allied in composition as those of which we have been treating.

En passant it may be pointed out that Harnack and Schmiedeberg write of 'lecithine from albumin.' In face of what has been heretofore advanced, this statement is evidently erroneous. Lecithine is derivable from brain matter, egg yolks, bile, and the roe of certain fishes, but it is in no instance obtainable from albuminous principles which are free from phosphorus.

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[1] *Deut. Chem. Ges. Ber.* vii. 1406.

[2] *Deut. Chem. Ges. Ber.* ix. 34–42.

The base obtained from brain matter, sometimes termed neurine and sometimes choline, is readily identified; its hydrochlorate is freely soluble in alcohol, from which solution an alcoholic solution of platinic chloride throws down a yellow powder which readily crystallises from hot water in delicate needles possessing the composition $2(C_5H_{13}NO)2HCl,PtCl_4$. The base possesses the further general characters of an alkaloid, and as such is amenable to such processes for isolation as that of Sonnenschein.

The Cerebrine Group.

This group of brain principles contains carbon, hydrogen, nitrogen, and oxygen, and all its members are readily soluble in hot spirit, recrystallising therefrom on cooling. By a process of fractionation several distinct substances may thus be isolated, their purity being indicated by a homogeneous microscopical character.

To free them from the myelines which obstinately adhere to them as isolated from the brain, it is best to continually re-dissolve them in successive quantities of hot alcohol until the deposits are quite free from phosphorus; the myelines remain in solution.

When placed in water they swell up enormously, but do not dissolve; they are insoluble in ether, cold benzene, and mainly insoluble in cold alcohol.

Three preparations made by Thudichum gave on analysis the empiric formulæ $C_{34}H_{66}N_2O_8$ (Müller), [illegible], and $C_{48}H_{91}NO_9$. To the first of these Thudichum reserves the name of cerebrine, the second he terms phrenosine, and the third kerasine.

When cerebrine in excess is heated in alcohol rapidly, a part of it fuses and then remains insoluble. This body—apparently an isomer of cerebrine and termed stearoconote by Thudichum—dissolves readily in benzene, and on addition of alcohol the original cerebrine is reformed.

As will be more fully explained in the Chapter on the 'Pettenkofer reaction,' all these substances give, with strong sulphuric acid alone, the violet colour which has been more particularly studied by Kingzett and Hake.

When boiled with baryta water, or heated therewith at 130° C. in sealed tubes, or preferably boiled with dilute sulphuric acid, all these cerebrines give glucose, a fact rendered previously probable by Liebreich's observations.

To this glucoside character is also probably due the fact that when heated to 160° C. these bodies fuse, become dark, and evolve water, just as sugar does in course of transformation into caramel. The strong affinity, moreover, they possess for water, as evidenced by the swelling therein, remind greatly of the starches which yield glucose also by boiling with dilute acids. The difference, however, between cerebrine and its varieties and ordinary glucosides or saccharides, consists in their contained nitrogen. Hitherto, the attempts made by Thudichum to isolate the nitrogenous nucleus or nuclei, have not been otherwise than partially successful. The method employed has been one of hydration carried out upon the mixed cerebrines, and the chief result the obtaining of a principle which seems to be only an intermediate product of considerable interest, and to which a provisional formula of $C_{25}H_{49}NO_8$ is given. Thudichum calls this substance 'pyschosine.'

Of the nature of the fatty acids whose radicles seem to form proximate nuclei in the individual members of this group of substances, we are as yet without knowledge.

Cerebrine, phrenosine, and kerasine, when recrystallised from hot alcoholic solutions, are deposited (in mixture) in minute balls or rosettes of a microscopical character, and crystalline in structure without being crystallised; that is to say, no definite geometrical form can be assigned to them.

Kerasine, when pure, may be obtained as a gelatinous membranous mass consisting exclusively of needle-like particles; and thus by continued and repeated fractionations of a mixture of the cerebrine principles, it may be obtained from the latest mother liquors in a pure state—that is to say, free from cerebrine proper and phrenosine which are deposited at earlier stages.

The substitution products of these principles have been but little studied, although Thudichum has ascertained that phrenosine, when treated with strong nitric acid, yields the nitrited body $C_{34}H_{66}(NO_2)NO_8,H_2O$.

Bromine also forms substitution products with these principles whose real formulæ may probably ultimately be definitely established by such products.

Cholesterine, Water Extractives, and Salts present in Brain Matter.

As cholesterine has already been studied and described in the Chapter on the Chemistry of Bile, it is unnecessary to refer to it here beyond pointing out that it forms a considerable constituent of brain substance. From its ready solubility in ether and hot alcohol it is easy to purify, and when associated with fatty matters or any of the phosphorised principles, it is readily freed from them by rendering the alcohol used for purposes of recrystallisation alkaline with caustic potash or soda; any colouring matter may be taken out by charcoal.

The water extracts of the brain contain a matter resembling, but not identical with, uric acid; a tribasic acid which is crystalline and yields a ferric salt; hypoxanthine ($C_5H_4N_4O$), and a base of the empiric formula (C_3H_4NO); also lactic acid in considerable quantity. Human brains seem to contain no inosite, which latter substance is a constant ingredient of ox-brain matter. Besides these principles and the salts of which we shall treat hereafter, other matters are contained and form perhaps the bulk of the extractives, but hitherto they have not been clearly elucidated. The presence of urea appears to be indicative of disease, and is not found in health. The alkaloids already mentioned, and others not yet defined, may be isolated by such precipitants as phosphomolybdic acid, tannic acid, iodine, mercuro-potassic iodide, mercuric chloride, silver nitrate, and auric chloride.

Hypoxanthine from brain matter is most readily purified by means of its silver nitrate compound, $C_5H_4N_4O+AgNO_3$, which readily recrystallises from hot nitric acid, and is a convenient salt for analysis.

The base $C_3H\ NO$ forms a gold salt, in which, however, the gold is more or less reduced to the metallic state during operations with it.

Lactic acid is obtained by strongly acidulating the concentrated water extracts with sulphuric acid, and extraction with ether. On distillation of the ethereal solution free lactic acid is obtained, and may be converted into soluble and crystallisable zinc salt by heating with the oxide or carbonate of that metal.

Inosite may be obtained by precipitation of the water extracts of ox brains with basic acetate of lead and decomposition of the precipitate suspended in water with sulphuretted hydrogen; on concentration of the filtrate the inosite ($C_6H_{12}O_6 2H_2O$) crystallises out and may be purified by recrystallisation.

It may not be out of place here to remark once more upon the applicability of Sonnenschein's method of isolating alkaloidal principles in such researches as those under consideration. The description of the process is best preceded by that of the preparation of the reagent. Molybdate of ammonium and phosphate of sodium are dissolved together in such proportions that thirty atoms of phosphorus are present for every one of molybdenum, and the resulting mixture is precipitated by nitric acid to perfection. The yellow precipitate thus obtained is dissolved in a strong solution of sodic carbonate, preferably containing a little caustic soda, and the whole evaporated to dryness, then fused, adding from time to time a little nitre so as to prevent any reduction of the molybdenum compounds. The product is one conveniently stored, and when required for use it is only necessary to dissolve it in water with the after-addition of nitric acid (diluted 1 : 6) until a golden yellow colour is attained. When it is desired to isolate or purify alkaloidal matters from any mixture, the solutions containing them are precipitated with the phospho-molybdic solution prepared as described, until a further addition of the reagent or of nitric acid gives no more precipitate. This latter is then separated by filtration, washed with water slightly acidified, first with nitric acid and afterwards with sulphuric acid, and then heated in the presence of excess of boiling strong baryta water. The mixture often turns blue at this stage, but is ultimately presented as a white precipitate (phospho-molybdate of barium) suspended in a yellowish solution containing the alkaloids. From this latter the excess of baryta is now removed by carbonic anhydride or the exactly necessary quantity of sulphuric acid, and there is thus obtained an ultimate solution freed from much impurity, and in a condition ready for any further methods of investigation.

Thudichum has remarked that certain alkaloids, such as those from brain matter, have not only the power of combining with acids and salts, but also with bases, in which case, where carbonic anhydride is used for removing the excess of baryta in the above process, barium salts remain and these are only decomposable by means of sulphuric acid. Thudichum describes such alkaloids as 'soluble ones, having simultaneous acid properties,' and since his observations many alkaloids have been observed to possess these characters; for instance, I noticed them in the case of pilocarpine which I have extracted from jaborandi.[1]

The inorganic principles of brain matter are interesting and numerous.

They comprise sulphuric acid, hydrochloric acid, phosphoric acid, and carbonic acid, all in combination with bases including potassium, sodium, ammonium, calcium, magnesium, copper, iron, aluminum, and manganese.

The function of inorganic salts present in the animal system has been by no means clearly made out; that they have an important one, however, there can be no doubt. Of this we shall treat more specifically hereafter, but it is convenient here to draw attention to a corresponding purpose served by saline matters in plant life. Liebig clearly proved that the minute proportions of these ingredients are individually and collectively as essential to healthy plant life as a supply of the most weighty constituents. So in like manner it is more than probable that those present in brain matter are as intimately connected with its important functions and are not present merely by accident. It is the more probable because, as has been already shown, they are more or less in combination with the actual organic principles of brain matter. It is perhaps less probable that the small amount of copper observed in the brain is useful in any way, nevertheless it is invariably present in traces, as is also manganese. How it gets there is not a matter of difficulty to understand; it may be absorbed into the system along with other mineral substances present in vegetables, and by the constant use of articles containing copper. The copper present in brain matter exists mainly, if not entirely, in combination with the phosphorised matters, so that if a quantity of crude kephaline be dissolved in water and precipitated by hydrochloric acid, the combination is split up, and the solution on examination will be found to contain copper.

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[1] *Journ. Chem. Society*, October 1876.

This is a fitting place to dwell upon the presence of the traces of copper which exists in brain matter and other animal tissues. There is no difficulty in recognising its presence in brain matter if sufficient material be operated upon. It is best detected by igniting dried brain substance with a fusion mixture of potassium carbonate and nitrate: in this way the organic constituents are destroyed, and there remains a fuse containing phosphate of copper which may be readily detected by the ordinary reactions. This circumstance reminds forcibly of the colouring matter, turacin, resident in the feathers of certain birds—*Calurus auriceps* and *Catinga cærulea*—which Church[1] found to contain copper in organic combination, and which is represented by the empirical formula $C_{50}H_{56}CuN_5O_{19}$. These birds, otherwise known as plantain-eaters, occur in regions containing much malachite in the soil, and it is conjectured that the copper thus found present in the pigment of their feathers is derived from the earth taken into the system while feeding. If this be so, it would seem that here the copper serves at least an useful purpose, if not a necessity of physiology. It is impossible to say whether the traces of copper present in brain matter serve any useful purpose, but that it exists there in combination with the phosphorised principles is beyond doubt. Moreover, Margraff, Gahn, and Vauquelin also observed the presence of the metal in organic tissues and products, and in 1856 and 1857 Odling and Dupré made a number of interesting experiments, in which they ascertained the presence of traces of copper in bread, flour, wheat, straw, liver, kidney, blood, flesh, eggs, cheese, &c. Thus they found that 6925 grains of human liver furnished 0·013 grain of cupric oxide; while 6682 grains of sheep's liver gave 0·281 grain CuO; 1830 grains of human kidney gave 0·015 grain CuO, and human muscle and blood gave traces.

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[1] *Transactions of the Royal Society*, xxi. p. 627.

More recently, Bergeron and Hôte[1] have demonstrated the presence of copper in the kidneys and livers of fourteen human bodies.

Of course there can be no doubt that the copper occurring in the human body must be mainly introduced by articles taken as food — an observation supported by Odling and Dupré's experiments and by the known facts that articles of food, such as preserved peas and pickles, often contain, and are, indeed, intentionally coloured with traces of copper added in the form of sulphate.

These traces thus occurring in foods do not find their way to any considerable extent into the system; that which is present in the body represents the accumulation effected during a number of years, dating from birth. It exists in organic combination with various principles, such as albumin, or the phosphorised brain constituents, and is thus, to a large extent, made stable and fixed.

Dr. Paul and myself made a number of experiments[2] upon this subject. Preserved peas containing copper were taken as food, and also repeated doses of sulphate of copper, to the extent of 0·467 grain each, daily; but a very small proportion of this copper was absorbed into the system, nearly the whole of it being excreted in the fæces. This is easy of explanation. After gastric digestion, and while the contents of the stomach are still acid, a part of the chyme is at once absorbed into the blood system, and this would seem to constitute the stage at which the copper is absorbed. The greater part, however, of the digested mass passes on through the pylorus, and undergoes a further change in the duodenum, when alkaline biliary fluid takes part in the process. The probable result, as regards any copper in a soluble state (and that not rendered soluble would not count) would be its precipitation as phosphate, which, being unchanged in the intestines, would pass out with the fæces. Of course, under certain conditions regarding amount, the quantity and acidity of stomachic contents, &c. &c., larger quantities of copper solutions would be poisonous, as an abnormal quantity could be absorbed; but the traces present in foods are absolutely innocuous, for the reasons above stated and particularly because (as Dr. Paul and I showed) the copper present in preserved peas exists in combination as an albuminate not easily digestible.

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[1] Comptes Rendus, [illegible], p. 268.

[2] *Pharm. Journal*, September 1877.

The Physiology and Pathology of the Brain from a Chemical Point of View.

With the aid of what has been stated in the preceding pages, we are now qualified to inquire regarding the life functions of the brain.

It has been shown that brain matter containing so much water is a kind of colloid septum, with a great mobility of character; further, its principles present affinities and powers of combination almost unequalled in chemical science. Kephaline, for instance, in aqueous solution is precipitable by nearly every reagent, including acids, bases, and salts like sulphate of copper and sodium arsenite. This power of combination can be overcome by much water, so that if these precipitates be placed upon a dialyser over water they give up again the respective combinants. The combinations with metallic oxides, as those of lead, copper, and iron, can only be undone by the agency of acids. On the subject of these affinities Thudichum writes—'The exercise of these affinities being greatly increased by the mass of reagent and the mass of water which may be present, the interchange of affinities may produce a perfectly incalculable number of states of the phosphorised, and consequently of brain matter. This power of answering to any qualitative and quantitative chemical influence we may term the state of *labile equilibrium*; it foreshadows, on the chemical side, the remarkable properties which nerve matter exhibits in regard of its vital functions. From this it also follows that nerve matter (if only as characterised by the phosphorised bodies) must yield obedience to every, even the slightest, external chemical influence which may reach it by way of the blood. It must take up metals, acids, salts, alkalies, and alkaloids presented by the blood; it can retain only oxides when the serum is again free from the combinants; a watery serum will wash the brain, a more watery one will make it swell, and displace mechanically, within physiological limits, what it can. A still more watery one will make the brain dropsical, and produce all the conditions of mechanical pressure on the brain. All these processes are the necessary consequences of the affinities of the phosphorised substances, and, these being known, the phenomena could be predicted if they were not sufficiently known as phenomena, though hitherto destitute of an explanation. Thus the so-called brain fungus—the continued protrusion of brain matter through apertures of the skull produced by mechanical injuries may, in certain cases, find a physical explanation in simple excessive hydration of the phosphorised (and nitrogenised) principles producing general intercranial pressure.'

Now if this be true, then in cases of poisoning by such metallic compounds as those of mercury and arsenic, these substances should be found in the nerve matter after death from such causes; and there are records bearing out the truth of this conception. D. Scolosuboff[1] has published experiments, in which he administered doses of sodium arsenite to dogs, rabbits, and frogs, which show that the poison concentrates principally in the nervous tissue, smaller quantities being found also in the muscles, liver, and marrow.

In further illustration of the meaning thrown upon pathology by means of physiological chemistry we may instance the disease known as softening of the brain. It has been pointed out that in cases of this disease glycerophosphoric and fatty acids are found in the brain in the free state; these substances never occur in health, but, curiously enough, they constitute the main decomposition products of the phosphorised principles. What other inference can be drawn except that, in softening of the brain, these principles are decomposed, and yield the substances whose presence characterises the disease? If such be true (and so it seems to be), it becomes possible to represent this disease by means of a chemical equation! I do not say this represents the beginning and end of the disease, the first cause—that may be remote in the extreme; but however this may be, the disease is revealed by a chemical change which we can express almost mathematically, and which may be imitated artificially in the laboratory.

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[1] *Bull. Soc. Chim.* (2) xxiv. 124.

Impressed with the possibility of chemical science to explain disease in some measure at least, I was led to consider that known as *delirium tremens*,[1] and, prepared by the knowledge regarding the brain set forth heretofore, I conducted some experiments to decide, as far as could be, the probability of my hypothesis. Before describing the results it may be profitable to go briefly over the work of others who have devoted themselves to the question of the action of alcohol in the body. All previous workers had confined themselves rather to a study of the *channels* through which alcohol might be supposed to act than to a study of the *action* itself.

In 1839 Dr. Percy published a research bearing upon this subject, and concluded 'that a kind of affinity existed between the alcohol and the cerebral matter.' The research was of an experimental nature, and Percy states that he was able to obtain a much larger proportion of alcohol from the brain than from a greater quantity of blood than could possibly be present within the cranium of the animals operated upon.

In 1859 Marcet (in a paper read before the British Association) endorsed the views of Percy, and reviewed the researches of L. Lallemand, Michel Perrin, and Duroy, 'who withdrew the blood from the brain in cases of poisoning with alcohol, and succeeded in extracting alcohol from the cerebral substance thus free from blood.' He also detailed some physiological experiments from which he concluded that 'alcohol acts *principally*, though not *exclusively*, on the nervous centres by means of absorption, and consequently through the circulation;' and that it also 'exerts a *slight* but *decided* action on the nervous centres through the nerves, independently of the circulation.'

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[1] *Chemical News*, vol. xxxiv. p. 158; and *Pharm. Journ.* February 26 and March 11, 1876.

The more general question regarding the fate of alcohol when in the system has been more extensively studied. Thudichum was the first to determine quantitatively the amount of alcohol eliminated by the kidneys from a given quantity of alcohol administered, and the result disproved the elimination theory then widely prevalent.[1] Dupré, Anstie, and others followed up these investigations, and the results of continued researches may be given in Dupré's own words:—

'(1) The amount of alcohol eliminated per day does not increase with the continuance of the alcoholic diet; therefore all the alcohol consumed daily must of necessity be disposed of daily, and as it is certainly not eliminated within that time, it must be destroyed in the system.

'(2) The elimination of alcohol following the taking of a dose of alcohol is completed twenty-four hours after the last dose of alcohol has been taken.

'(3) The amount eliminated in both breath and urine is a minute fraction only of the amount of alcohol taken.'

All these researches had reference to quantities of alcohol below those the consumption of which produces *delirium tremens*, and in any case the fact that alcohol is not eliminated does not prove what becomes of it. Of course, in process of time, it becomes entirely oxidised, but, until that has been entirely effected, where is the alcohol resident? Is it distributed equally throughout the circulation, or, as evidenced by Percy's experiments, does it find a special lodgment in the brain? If so, by what power, and while there how does it produce the disease *delirium tremens*? These were the points to which I devoted myself in the research which I communicated to the British Association meeting at Glasgow (1876). To understand the experiments made, it is necessary to recur again to what has been advanced regarding the molecular state of the brain in health. It is a large, mobile, penetrable, colloid septum, which is subject to every influence reaching it by way of the blood, and exhibiting a great power of combination. A large percentage of alcohol in the blood may therefore be conceived to act upon it by robbing it more or less of its mobile character which is essential to its healthy functions, and consequently by impairing its power of assimilating food and throwing off the products of its work; or alcohol may be supposed to act by dissolving traces of the principles of which brain matter is composed—albumin, kephaline, myeline, lecithine, cerebrine, cholesterine, &c. It is unnecessary to give here the details of my experiment; it will be sufficient to state the method and the main results. The method employed, consisted in suspending whole ox brains, freshly removed from the skull, in watery solutions containing from 6 to 50 per cent. of alcohol, and maintained at the temperature of the blood during a number of hours. The extracts thus obtained were evaporated down, and the dissolved matters weighed and submitted to careful analysis. In some cases also the specific gravity of the brain before and after the experiments was noted. The result was seen to be that alcohol has no more chemical effect on the brain matter than water itself, so long as it is beneath a certain proportion to the total quantity of liquid; but if that proportion be exceeded, the brain principles, including kephaline, begin to dissolve and pass into solution, while the specific gravity of the brain is at the same time affected both by the loss of matter and the assimilation of water or alcohol. Thus in one case where water only was employed, the specific gravity changed from 1036 to 1007; this was due to swelling, as the brain had not materially altered in weight. In a second experiment (with a solution containing 38 per cent. alcohol), the specific gravity changed from 1031 to 1005; here the brain had gained materially in weight, and suggests that alcohol was absorbed mechanically. Water itself has a decided action upon the brain thus treated, and, like more dilute alcoholic solutions, dissolves cerebrine, myeline, &c., but no kephaline. The serum, rich as it is in salts, prohibits the action of water as such upon the brain in life; but, on the other hand, it is not easy to see how any of the matters we know to exist in the blood could prevent alcohol, when present in sufficient quantity, either from hardening the brain or from dissolving traces of its substance, to be henceforth carried away in the blood. It would not be wise to draw any final conclusions from this investigation until it has been supplemented by others of a like nature and supported by further physiological researches. The facts irresistibly remind of the words of Shakspeare, 'O that men should put an enemy in their mouths to steal away their brains.' I would not, however, be understood to condemn the proper use of alcohol; indeed, in my opinion, in spite of many statements lately made to the contrary, it is to be regarded as at once a luxury and an useful article of diet. It is matter of deep regret with me that no opportunity has been afforded of following up the researches here briefly indicated. Some good results might be obtained by administering large quantities of alcohol to horses intended to be killed, and distilling their brains, removed immediately after death. If alcohol were obtained in any quantity, it would clearly substantiate the conception that the brain has a retentive power for that substance.

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[1] *Practitioner*, March 1872.

The Brain in Typhus and other Diseases.—In commenting upon Thudichum's researches on the chemical constitution of the brain, Mr. John Simon (then Medical Officer of the Privy Council and Local Government Board) writes:[1] 'Especially a leading fact in typhus, one which may be in intimate relation to the killing power of the disease, and which it is on all accounts necessary to have as completely as possible understood, is the fact of the action on the nervous system; and clearly no true knowledge of that morbid action would be possible till greatly improved knowledge of the normal brain chemistry should be supplied.'

Not only is the brain and nervous system directly affected by or concerned in all diseases, but even the questions of thought, imagination, and intellect are deeply connected with the brain, and therefore with its chemical constitution among other factors; but the connection is, more than all things else, at present remote from our knowledge. Of course we must never lose sight of other considerations affecting the brain, as, for instance, structural form, functional localisation, bulk, and weight.

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[1] *Report of the Med. Off.* &c. New Series, No. iii. p. 8.

Liebig broached the idea that every functional act, whether muscular, cerebral, or otherwise, was necessarily attended by the destruction of living cells. More recently, we have seen that Dr. Gordon Hake has contested this theory, and has insisted upon the view that the cerebro-spinal system does not generate its own force but derives it through the chemical changes in the lungs; and it is certain that Frankland's experiments which have been described in another chapter, support this view.

If the exercise of the brain and nervous powers were attended with the destruction of their own matter, and even supposing that they were kept supplied with new substance formed from the nutrient blood; the elimination of phosphates from the breaking up of the phosphorised principles would probably far exceed in amount that which may be observed. But to return from this digression.

So far as the pathology of the brain has been studied, the diseases to which it is subject may be classed under two headings, namely (1) Diseases of the membranes, and (2) Diseases of the brain substance.

Thickening of the walls of the sinuses of the membranes, and arterial ossification of the brain, are complaints which have yet received no kind of elucidation.

Tumours sometimes form both in the membranes and the brain substance, and the intercranial pressure thus often generated gives rise to paralysis, convulsions, apoplexy, &c. When these tumours are situate near the base of the brain they affect the mental state, sensation, and volition, obscure the intellect, and often produce idiocy. Otto has described a tumour (from which the Duke of Saxe-Gotha suffered) six inches long and three broad, found in the right hemisphere, and Esquirol states that he observed a tumour containing fat. Unfortunately we have no knowledge of the chemistry of tumours and cancerous growths, and thus it is impossible even to speculate on the way in which they arise.

Meckell has recorded a case of phthisis in which the density of the brain was sensibly diminished, and this would point to some extent to the same cause as hypertrophy is due, namely to a swelling of the brain through the agency of a watery serum.

Induration or hardening of the brain is a commonly observed fact in many cases of typhus and other fevers.

'Locomotor ataxia' is a curious disease which appears to have its origin in a degeneration of the spinal marrow; the sense of pressure is partially or entirely lost, although the susceptibility to heat, cold, pain, &c., remains. In this disease a peculiar matter termed 'amyloid' is found in the marrow substance, and this gives with iodine a blue coloration like that given by starch. It may be that this substance is a decomposition product of cerebrine; indeed that substance which, when cerebrine is subjected to hydrating agents, gives rise to the production of sugar (glucose).

But without dwelling further upon the pathological chemistry of the nervous tissues, a subject as yet all but entirely neglected, we may conclude by saying that so far as processes of hydration, oxidation, &c., can occur in the living body, be they characteristic of health or disease, so far will the products be those which may be similarly obtained in the laboratory, and hence we perceive the necessity of a thorough study of brain chemistry. Already we know enough of this subject to enable us to trace the changes characteristic of many diseases; the declensions from those standards which are the measure of health; but this knowledge is nowhere applied. What is particularly needed, and what might with considerable ease be effected, is this:—Cases of disease affecting in any manner or measure the brain, should be registered, and the brains after death submitted to investigation. This investigation should of course have its histological side—and, indeed, this matter is already carefully attended to—but it should also have its chemical side. The weight and specific gravity should be carefully ascertained, and then a qualitative and quantitative examination should be instituted, keeping watch specially for anything abnormal or not previously recognised, and notably for those decomposition products of the phosphorised and other principles peculiar to nervous tissue and derived therefrom by the methods of change which have been described, with their results, in previous pages. In the meantime, what is urgently needed is an accurate determination of the relative amounts of those constituents we have described as occurring in brain matter, and the difference exhibited in the quantitative composition of white and grey matters and of nerves.

CHAPTER XVI.

OTHER ANIMAL ORGANS, TISSUES, AND SOLIDS.

The Thymus Gland.

THE *thymus* gland is situated at the base of the heart, in front of the lungs. It consists of an aggregation of follicles like those found in the small intestine; it is largest in infants, and, according to Huxley, gradually disappears in adult and old persons; its framework is albuminous, and it contains a little fat, leucine, xanthine and hypoxanthine, succinic and lactic acids. Thudichum states that in the progress of involution of the thymus the amount of sodium it contains is nearly doubled. Of the function and chemical history of this organ next to nothing is known.

The Thyroid Gland.

The *thyroid* gland, like the *thymus* gland, is abundantly supplied with lymphatics; it lies in that part of the throat below the larynx, and is subject to a disease by which it becomes enlarged, giving rise to 'goître' or 'Derbyshire neck.' Its ingredients, so far as they are known, are like those of the thymus and other glands of different situation. It is said also to contain mucin, and in certain diseased states cholesterine is present. Its chemical constitution and function are for the most part undetermined.

The Supra-renal Capsules.

The supra-renal capsules which lie above the kidneys also exercise an unknown function. They seem to contain an imperfectly studied matter which Thudichum terms *renculine*, a substance which communicates to alcoholic or ethereal extracts a yellow colour which darkens to red on exposure to the air. Such solutions exhibit a green fluorescence. Iodine gives a red colour to the watery extracts of supra-renal capsules, and ferric chloride strikes therewith a blackish-blue colour. The supra-renal capsules also contain leucine, and seem to be particularly concerned in Addison's disease, or 'bronzed skin.'

The Ovaries.

The chemistry of the ovaries is in a very unsatisfactory condition. The *corpora lutea*, of which they are in part composed, contain fluid in which the presence of coagulable serum may be detected. They also contain a granular substance termed luteine, which is a yellow colouring matter soluble in alcohol, ether, and chloroform. Thudichum points out that the spectrum of its solutions consists of three absorption bands in the blue and violet, and is similar to that presented by apparently the same principle contained in yolk of eggs. An albuminous fluid, which also exhibits this spectrum, is said to be contained in some forms of ovarian cyst. Further, a somewhat similar colouring matter is, according to Thudichum, contained in the yellow fæces of sucking infants.

Muscular Tissue and Extract of Meat.

The tissue of voluntary or striated muscles, and that of involuntary or smooth muscles, are no doubt to a large extent composed of the same principles; at the same time it is probable that as physiologically considered the functions of each are not precisely similar, so also certain differences in their chemistry will be elucidated when they have been better studied and when the methods of chemical science shall have been more perfected. As it is, chemical studies have rather confined themselves to the striated muscles. These are made up of disks or tubes of syntonin—a peculiar contractile albuminous principle—imbedded in a sarkolemma or membranous sheath, and surrounded by a semi-fluid plasma.

Muscular tissue, then, consists of about 75 or 80 per cent. of water, and 15 or 17 per cent. of certain albuminous principles, while the rest is made up of certain so-called extractives and salts.

The syntonin, or solid part of the flesh—sometimes termed flesh fibrin—is insoluble in water but can be extracted from the insoluble part of meat by means of dilute acids in large quantities. Dissolved in the plasma of the muscles are a number of albuminoids more or less closely related to this syntonin. Some of them no doubt represent the pabulum out of which the solid part of the muscle is constructed, while again others are derived from the syntonin by processes innately associated with physiological processes. Thus the plasma contains a substance of which mention has been made elsewhere, viz. myosin; this may be obtained by pouring plasma into warm water, when it coagulates. Myosin is like fibrin in many respects and among these in its power of decomposing peroxide of hydrogen by contact; in fact, myosin is transformed (apparently) into syntonin by treatment with dilute acids. There are also present in plasma; potassium-albumin, seralbumin, and myochrome, which is (according to Thudichum) identical with hæmato-crystalline of the blood. Myochrome is absent in white muscular tissue.

Although the plasma is alkaline when fresh, meat when kept quickly becomes acid; and Thudichum explains this as due to the formation of paralactic acid which at first shares the potassium of the phosphate and transforms it into acid phosphate. 'Only when excess of paralactic acid in its free state is present, does the albumin separate from the potassium albumin' (Thudichum[1]) of the muscle serum, or plasma freed from myosin.

The soluble constituents of muscular tissue may be obtained by extracting minced meat with cold water and separating the albuminous parts of the extract by boiling, which causes their precipitation. The fluid then contains the soluble salts found in the blood, kreatine, kreatinine, inosite, uric acid, xanthine, hypoxanthine, taurine, glycogen, sugar, inosic and paralactic acids, formic, acetic and butyric acids, and other substances by no means well made out.

In fact, while flesh yields about 1·25 per cent. of extractives, we are only acquainted with the nature of 0·21 per cent., or about a sixth part of the total quantity. This knowledge is chiefly the result of Liebig's researches, the practical outcome of which may be said to be the commercial preparation of a so-called extract of meat, or beef tea, which often proves of great dietetic value to both healthy and sick persons. This extract of meat contains about 18 per cent. of salts (chiefly potassium compounds) and about the same percentage of water.

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[1] *Chemical Physiology*, p. 36.

We have seen that Liebig was only successful in ascertaining the nature of less than 17 per cent. of the total matters entering into the composition of this extract. 'Fortunately for science, Liebig was more conscientious than many workers in this direction; for it is a weakness, not only on the part of the physiological chemist but on that of the ordinary chemist, in their investigations to seize upon one particular product, preferably choosing the most crystalline, and to examine it to the neglect of the 99 per cent. This would not be of so much import if at the same time it were accompanied by a statement of the fact, but as it is, their publications are not rarely so worded as to convey to the mind of the reader imperceptibly the idea that nothing remains to be done.'[1]

That the muscle may be said to transform chemical force into mechanical force there can be no doubt, but it is not so clearly established that this chemical force is generated *in* the muscles themselves. In the Chapter on 'Animal Heat and Vital Force' certain different views held upon this matter have been already discussed, and it is therefore needless to repeat them in this place.

The presence of a colouring matter in red muscles, similar to the hæmato-crystalline of the blood, is certainly significant; and various researches, particularly those of Brown-Séquard, have demonstrated that the contractibility of the living muscle is dependent upon the circulation of arterial blood. Hence it is not improbable that by combination of oxygen conveyed by the blood with this colouring matter of muscles, a quantity of this gas is stored therein, and may serve by the oxidation of oxidisable substances to generate force *in situ.* The large dependence of muscular action upon the exercise of will tends, however, to show that the mechanical force is directly due to a cerebric force, having of course its primary origin in the oxidation occurring in the blood. The loaded muscle is alkaline, but becomes acid during work, in which operation carbonic acid is liberally set free, although muscular exercise does not appear to greatly increase the amount of urea excreted. It thus seems that the albuminous compounds do not suffer disintegration in the muscles to any large extent, but rather that the process of oxidation occurs chiefly upon the carbohydrates. Nevertheless the presence of kreatine and other nitrogenous matters previously enumerated, points on the other hand to a characteristic decomposition of albumin. Of course the measure of carbonic acid given off is a measure of the muscular activity, and consequently this is a less quantity when the muscle is at rest than when it is contracted. This contracted state is also characterised by an acid reaction.

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[1] See Essay by Kingzett and Hake, *Quarterly Journal of Science*, January 1877.

Kühne has demonstrated that *rigor mortis* is due to the separation and coagulation of the myosin contained in muscle plasma. So soon as this myosin softens and disintegrates, the rigidity ceases. 'The muscle participates in all febrile diseases of the body, and is frequently the seat of idiopathic processes.' (Thudichum.)

In typhoid, typhus, and other fevers, it degenerates in structure and becomes yellowish; in fatty degeneration it loses its contractibility, and fat may then be detected in the free state; in trichiniasis it is the seat of the *trichina spiralis*. In other diseases the muscle is likewise seriously affected, but in what precise manner or measure cannot at present be stated.

The chemical constituents of muscular tissue have been for the most part particularised in other places, and it is only necessary here to give the chief characters of inosic acid which is peculiar to muscular tissue. Under the constituents of urine we have described a method for extracting kreatine from flesh of fowl, &c. It is from the mother liquors after the removal of kreatine that inosic acid may be best obtained. The liquors are concentrated and then treated with alcohol till a milky appearance is obtained; they are then allowed to stand and crystallise. The crystals of barium and potassium inosates thus obtained are dissolved in hot water and more barium chloride added, so as to get all the inosic acid as barium salt. This done, the salt is crystallised out; and by recrystallisation and subsequent decomposition with sulphuric acid, pure inosic acid is obtained.

Inosic acid ($C_5H_8N_2O_6$) is an uncrystallisable syrupy matter, easily soluble in water; it is precipitable from its watery solution by alcohol, and is insoluble in ether. The salts of the alkalies are crystallisable. The copper salt is insoluble in acetic acid, but dissolves readily in ammonia. The taste is pleasant, reminding of the juice of meat, and when burnt it gives off the odour of roast meat.

Before concluding this chapter we may remark that many years ago H. Vohl showed that when inosite is fermented with putrid cheese or flesh it yields ordinary lactic acid. Hilger, however, disputed this statement, and alleged that paralactic acid was produced under these circumstances. More recently Vohl[1] has published some further researches upon this question with the result of confirming his former statement, and therefore removing Hilger's objection. The formation of lactic acid from inosite is the more interesting, bearing in mind the fact that inosite and paralactic acid are found together in the muscular tissue and in the brain matter. Whether the acid is formed from the sugar in the living body it is impossible to say, but it is certain that inosite often changes into an acid substance during certain chemical operations designed to extract it from animal matters.

The Bones.

The bones consist of so-called ossein—a peculiar albuminoid—associated with certain inorganic principles to which osseous tissues owe their rigidity. The other matters which are found occurring in or with bones, such as marrow, a little fat, vascular and fibrous threads, &c., are mere accessories to the tissues proper. More important, perhaps, are the cellular nuclei which are found in the cavities, and termed bone corpuscles. The external surface of bone, as also the internal surface of the cylindrical bones, is covered with a membrane or periosteum endowed with numerous nerves and vessels. This periosteum, like the ossein itself, yields gelatin by boiling.

When bones are treated with dilute hydrochloric acid during a protracted period, the earthy carbonates and phosphates are dissolved out, leaving a skeleton of the organic matter which retains the original shape of the bones—that is, of a tubular centre round which are disposed successive concentric layers.

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[1] *Deut. Chem. Ges. Ber.* ix. 984–987.

Dry bones contain about 29 to 30 per cent. of ossein, which when dissolved in hot water, yields gelatin. The inorganic matters combined with ossein in bones amount to about 68 or 69 per cent., and these proportions occur with some regularity, although by no means with perfect regularity. In fact, the amount of calcareous salts varies to some extent in different bones, at different ages, and under varying conditions of life.

The average composition of dry bones may be expressed as follows:—

Water and ossein, from	30	to	34	per cent.
Calcium phosphate ($Ca_3P_2O_6$)	45	,,	52	,,
Calcium carbonate	6	,,	14	,,
Calcium fluoride	1	,,	2	,,
Magnesium phosphate	0·8	,,	1·2	,,
Other salts containing some sodium chloride	traces			

The following analysis of human bone is by Berzelius:—

Water and cartilage (ossein)	32·17
Vessels (associated organic matter)	1·13
Phosphate of calcium	51·04
Fluoride ,, ,,	2·00
Carbonate ,, ,,	11·30
Phosphate of magnesium	1·16
Sodium, with a little chloride	1·20
	100·00

Von Bibra, in an elaborate treatise on the bones, gives numerous analyses, which bear out the fact above stated to the effect that the composition of bones, although approaching a general kind of regularity, is variable within certain limits; so variable indeed, that the idea of bone as a chemically individual substance cannot be entertained. The following analyses are selected from various sources, and are given, together with the authors' names.

	Man. Fore-arm. By Hersitz.	Femur of male fœtus at 6th month. Von Bibra.	Femur of man aged 51. Von Bibra.
Animal matter (ossein)	31·11	40·38	31·47
Calcium phosphate	59·14	53·46	58·23
„ fluoride	2·23		
„ carbonate	6·32	3·06	8·35
Magnesium phosphate	1·20	2·10	1·03
Other salts	—	1·0	0·92

Von Bibra's analyses seem to indicate that in young bones the organic matters are proportionately greater to the inorganic matters, which are therefore proportionately less, than in the properly developed bones of adults.

It has been stated above that at various times bone-substance has been regarded as a chemical individual. This idea derived particular support from some observations which were made showing that a mixture of gelatin and bone earth in dilute hydrochloric acid, when neutralised by ammonia, yields a deposit of phosphates containing about 20 per cent. of gelatin. Also, when a similar solution is mixed with tannin solution, tannate of gelatin containing bone earth is precipitated. But the variability in composition of osseous tissues is against the idea in question. Nevertheless that the earthy matters do undoubtedly exist in chemical combination with the ossein, is proved by the fact that bones do not suffer change when merely boiled in water—the ossein is not dissolved out. On the other hand, when placed with water in a Papin's digester and exposed to 150° C. for some hours, the gelatin is dissolved and the earthy matters disintegrate and remain insoluble.

Bone earth contains about 87·7 per cent. of calcium phosphate ($Ca_3P_2O_6$), 9·1 per cent. of calcium carbonate ($CaCO_3$), 3 per cent. of calcium fluoride (CaF), and 1·7 per cent. of magnesium phosphate.

When subjected to dry distillation, bones give off a quantity of fœtid, volatile, and tarry matters containing certain ammonium compounds—the products of the destruction of ossein—and yield a residue of animal charcoal. This residue contains of course the inorganic part of the bones more or less changed by the decomposition, in part, of the carbonate, and when strongly ignited in the open air the carbon may be entirely burnt off. On the other hand, the greater part of the inorganic matters may be dissolved out by acids, and in that case tolerably pure carbon is obtained.

When certain dyes, such as madder, are given with the food, they find their way into the bones which thus become coloured. From the mode in which this colouring occurred, it was inferred that the bones are rapidly renewed from without, but Thudichum considers this doctrine to be untenable.[1]

R. Maly and J. Donath[2] state that 100,000 parts of water dissolve about 2·36 parts of gelatinous calcium phosphate, 2·56 of calcined calcium phosphate, and 3 parts of calcium phosphate from powdered bones, but at what temperatures is not stated. They also observe that ossein when kept in contact with calcium phosphate, does not combine with it; and on this ground, and from the further fact that other albuminoids—such as ovalbumin and seralbumin—besides ossein are precipitated together with earthy phosphates from the same solution (with ammonia as above described), the authors conclude that bone is merely a mechanical mixture. We have already given reasons for regarding bone as in some measure at least a chemical combination (although not a chemical individual), and the experiments of Maly and Donath appear to have no direct bearing, in our opinion, upon this question.

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[1] *Chemical Physiology*, p. 47.

[2] *Journ. pr. Chem.* (2) vii. 413–440.

C. Aeby[1] regards bone as made up in great part of a complex molecule in which the lime and phosphoric acid bear a constant relation, but in which the excess of lime over orthophosphate sometimes wholly exists as carbonate and sometimes as partly carbonate and partly hydrate. All other authors, however, agree that the hydrate does not occur in fresh bones; and in a more recent paper F. Wibel[2] has criticised C. Aeby's researches, and concludes from his own experiments that the conclusions of the latter worker are arbitrary and erroneous.

F. Papillon[3] has published some interesting experiments upon the modifications that can be induced in the composition of bones. By feeding pigeons and chickens with an appropriate diet, he has succeeded in getting small quantities of magnesium salts taken up by the bones; and from these and formerly published researches he concludes (with no real show of reason, however), that metals like magnesium, strontium, and aluminium are assimilated in bone tissue in the proportion of their atomic weights. He compares quantities of the oxides against ratios of the metals, and thus Al_2 comes to be compared with Mg. Moreover, there are mistakes in his calculations, so that while the interest of the facts remains his conclusions may be entirely dismissed.

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[1] *J. pr. Chem.* (2) vii. 37–44.

[2] *Ibid.* (2) ix. 113–132.

[3] *Compt. Rend.* lxxxv. 352–355.

J. König has described[1] some experiments of a similar character. He relates how H. Weiske asserted, and Papillon denied, that animals fed on a diet containing phosphate of strontium get this compound deposited in their bones, and then proceeds to give his own experiments made with guinea-pigs. These demonstrate that strontium phosphate may thus replace phosphate of calcium, but he did not succeed in similar experiments conducted with aluminium phosphate.

Bones in Disease.—There are numerous diseases in which the bones are most seriously concerned, and become either brittle or singularly soft.

Thus, in rachitis or rickets—or, as the Germans term it, *cranio-tabes*—(a disease to which children are more particularly liable), and in osteomalacia of pregnant women and aged persons, the bone earth falls to an alarming extent, the ossein rising proportionately. The following analyses are instructive :—

Name of Disease . .	Rachitis			Osteomalacia		
Name of Bone . .				Vertebra	Scapula	Femur
Author	By Lehmann			By Bostock	Bogner	Lehmann
Components.						
Animal matter .	54·14	60·14	58·77	79·75	65·85	48·83
Calcium phosphate ,, fluoride	32·04	26·94	28·13	13·60	26·92	17·56
,, carbonate .	4·01	4·88	3·75	1·13	0·98	3·04
Magnesium phosphate . . .	0·98	0·81	0·87	0·82	5·40	0·23
Salts (soluble) .	0·75	1·08	1·01	4·70	0·85	0·37
Fat . . .	5·84	6·22	6·94	—	—	29·18

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[1] *Zeitschr. f. Biologie*, x. 65–72.

Name of Disease . . .	Arthritis	Chronic Gout	Caries	Necrosis	Sclerosis in high degree
Name of Bone . . .	Femur		Metacarpal	Phalanx	
Name of Author of Analysis	Marchand	Lehmann	Von Bibra	Von Bibra	Ragsky
Components.					
Animal matter (ossein)	46·32	38·14	37·97	19·58	38·27
Calcium phosphate and fluoride . .	43·00	35·16	49·77	72·63	61·47
Calcium carbonate .	8·24	8·41	7·24	4·03	
Magnesium phosphate	1·01	1·31	1·11	1·93	
Other salts . . .	2·00	2·93	0·30	0·61	0·26
Fat	—	12·11	3·61	1·22	—

It will be seen from these analyses, which are selected from a large number published by various workers, that the chemical composition of different bones in various diseases is a matter of extreme importance in helping us to obtain a more complete knowledge of the pathological processes. Thus, the high amount of calcium phosphate in the bones in necrosis is peculiarly significant, as is also the large percentage of fat which figures in chronic gout.

In rachitis, lactic acid has been found in and about the bones, and it is supposed that the diminished quantity of inorganic matters present in bones in this and similar diseases, is due to the solvent action of such acid. The question of course next arises, where does the lactic acid come from? To this question no answer can yet be given; and, in fact, we are in profound ignorance of the processes upon which these various diseases depend. It may be fairly anticipated that with a better general knowledge of them and the more assiduous application of chemical science to healthy and morbid parts of the body, our ignorance will gradually give place at least to intelligence, if not to knowledge and an exalted power of healing.

Teeth.

The teeth have a composition much like that of ordinary bones; and, indeed, the roots or stumps of teeth are bones properly so called. The exposed parts of the teeth, however, consist of many minute tubes of peculiar construction, and composed of what is called dentine; over this there is a harder epithelium structure termed cement. The enamel is deposited on the dentine in vertical layers, and it contains even less organic matter than the cement. The dentine hardly differs in composition from true bone, as the following analyses show:—

	Berzelius.	Von Bibra.	
Animal matter (ossein)	28·0	20·42	27·61
Calcium phosphate „ fluoride	64·3	67·54	66·72
„ carbonate	5·3	7·97	3·36
Magnesium phosphate	1·0	2·49	1.08
Salts (soluble) and fat	1·0	1·58	1·23

The cement contains about 4 per cent. of organic matter, 92 per cent. of earthy phosphates, and 4 per cent. of calcium fluoride. The following analyses are of enamel:—

	Berzelius.	Von Bibra.	
Phosphate of calcium Fluoride „ „	88·5	81·63	89·82
Carbonate „ „	8·0	8·88	4·37
Phosphate of magnesium	1·5	2·55	1·34
Membrane, ossein, fat, salts	2·0	6·94	4·27

From many analyses made by Lassaigne it would seem that the phosphate of calcium gradually increases with age, and that the amount of carbonate correspondingly falls:[1]—

	Organic Matter.	Phosphate of Calcium.	Carbonate of Calcium.
Tooth of child 1 day old	35·00	51·00	14·00
„ „ „ aged 6 years	28·57	60·01	11·42
„ „ an adult man	29·00	61·00	10·00
„ „ a man 81 years of age	33·00	66·00	1·00

The Nails and Hair.

The nails and hair admit of joint description because they are grouped together with other descriptions of horny matter which reveal chemical characters approximating both to those possessed by ordinary albuminoids and so-called gelatigenous substances. Both nails and hair may be viewed as metamorphosed epidermal tissue.

The Nails.—The bed of the nail consists of a vascular integument covered with growing epidermic cells, which flatten as the nail grows upwards and form the continuous horny plate of the nail proper. The nails grow from below and behind.

The following analysis of human nails is by Mulder:—

C. . . . . = 50·3
H. . . . . = 6·9
N. . . . . = 17·3
S. . . . . = 3·2
O. . . . . = 22·3

The Hair, like the nails, is composed of coalesced horny cells, but from the fact that the hair sac is in communion with sebaceous glands, it is thus kept supplied with a sort of natural pomatum; 'moreover, delicate unstriped muscular fibres are so connected with the hair sac as to cause it to pass from its ordinary oblique position into one perpendicular to the skin when they contract' (Huxley). These delicate muscular fibres contract sometimes under the influence of extreme terror, and thus give rise to the 'standing of the hair on end,' a phenomenon which further demonstrates that even the hair is in proper communion with the nervous system.

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[1] See Simon's *Animal Chemistry* (Dr. Day's English edition); Von Bibra's work entitled *Chemische Untersuchungen über die Knochen und Zähne des Menschen und der Wirbelthiere*; and Fremy's paper in *Annales de Chimie*, iii. xliii. 47.

The following analyses of hair illustrate its composition:—

	Van Laer.	Scherer.	Von Bibra.
C.	50·65	50·62	
H.	6·36	6·61	
N.	17·14	17·93	
S.	5·00	24·84	In some specimens of red hair 8·00
O.	20·81		

Hair also contains from 0·75 to 2 per cent. of ash, consisting, according to Van Laer, of chloride of sodium, sulphate of calcium and sulphate of magnesium, phosphate of calcium, ferric oxide, and silica. He considers that the iron is chemically combined with the organic matters and generally amounts to about 0·4 per cent. calculated upon the hair. It is just possible that the sulphates which he found in the ash were produced in the ignition of the hair by the oxidation of the sulphur in the presence of bases.

It is not clearly determined how far the colour of the hair depends upon chemical composition, or upon the nature and quantity of the natural animal fluid which bathes it, or upon the ultimate molecular arrangement of the hair substance itself.

The colour of the hair is affected by various metallic and other solutions, and the presence of sulphur is supposed to be associated with the cause of such changes.

Scherer and Van Laer state that by extracting hair with alcohol, ether, and water, they succeeded in obtaining margarin, margaric acid, olein, a brown soluble matter, chlorides of potassium and sodium, and lactate of ammonium.

Although the composition of hair and nails is nearer to that of ordinary gelatin than albumin proper, yet the reactions of these matters are more closely allied to the latter. They are stained yellow by nitric acid, become soft when heated, and when burnt give off a peculiar odour. The sulphur is partially removed by treatment with caustic alkalies; and the alkaline solutions thus obtained, when neutralised by acids, give an albuminous sort of precipitate. The cells and nuclei of hair and nails are rendered visible by careful treatment with a strong solution of potash.

W. R. Hodgkinson and H. C. Sorby have published [1] an interesting note on 'pigmentum nigrum,' or the black colouring matter of hair and feathers. Colourless hair and feathers dissolve entirely to colourless solutions when boiled with dilute sulphuric acid; but, on the other hand, when they are black or brown they yield a brown or red solution, and leave an undissolved black amorphous substance approximating in composition to albumin. The feathers of the common rook are stated to be the best source of this pigment, but unfortunately the authors do not explicitly state which substance they allude to. Whether therefore they are treating of the soluble or insoluble principle is left undecided, but they probably refer to the insoluble principle in the following analyses :—

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[1] *Journ. Chem. Soc.* April, 1877.

A mean of 10 analyses of pigment from several species of corvus, gave . . .	C. 55·4; H. 4·25; N. 8·5
Ciconia alba (mean of two) gave . . .	C. 55·5; H. 4·8; N. 8·5
Corvus pica „ „ „ „ . . .	C. 49·5; H. 4·8; N. 7·6

The simplest formula to be derived from these analyses is $C_9H_8NO_4$; the substance is probably a derivative of albumin, and of much greater complexity than this formula indicates.

Cartilage.

Cartilage is the name given to the white, horny, and elastic substance of which the articular extremities of bones are composed. It contains from 3 to 6 per cent. of saline matters, and by long boiling with water is transformed into chondrin—a tremulous jelly—similar to gelatin in many respects. It is, however, insoluble in acetic acid, and when boiled with hydrochloric acid yields sugar. The transparent cornea (hyaline variety), 'the rings of the trachea, the elastic parts of the ears, nose, and eyelids, and the flexible prolongations of the ribs, are also composed of the same material' (Miller). Cartilage is subject to a process which ends in ossification.

Connective and Elastic Tissue.

Connective tissue (also called *fibrous*, *areolar*, or *cellular*) connects the various organs of the body together, forming tendons, fasciæ, ligaments, skin, &c. &c. It consists of bands or cords or sheets of a wavy fibrous appearance (under the microscope). According to Thudichum it is soaked with potassium-albumin, and is thus described[1]: 'It consists of fibres, of a cement uniting these to a tissue, of cells or so-called corpuscles, and is interspersed with elastic fibres.' The cement dissolves in lime water or baryta water, and from these solutions acetic acid reprecipitates mucin or a substance identical with the constituent of the salivary glands and described under that name. Mucin resembles chondrin (of the cartilages) in so far that by boiling with dilute acids it yields sugar; it is also a good source of tyrosine, yielding 7 per cent. of that substance.

The fibrillæ of connective tissue yield gelatin when boiled sufficiently long with water or when treated with acetic acid, in which solution they swell up and become transparent. The filaments of elastic tissue resist this treatment.

Elastic tissue predominates in the yellow ligaments of the vertebræ, the sarcolemma of the muscular fibres, and neurilemma of the nerves.

The cells or corpuscles contain protoplasm. This latter is frequently stained with pigment of a black or brown colour, as in the choroid, the iris, bronzed skin disease, freckles, and more particularly and naturally in the negro skin. It is not unlikely that this colouring matter is similar to that of hair and feathers.

Ear Wax, or Cerumen.

This substance is secreted by the *glandulæ ceruminosæ*, 'situated in the external skin of the meatus auditorius externus' (Simon).

Ear wax is a yellowish mass made up of variously grouped lamellæ containing some pavement epithelium. Besides these it contains fat vesicles and sometimes rhombic crystals resembling cholesterine in appearance. The yellow colour is the property of that part of the wax which is soluble in water. The fat which Berzelius extracted from cerumen by ether contained stearin and olein, and gave (by proper treatment) a mixture of fatty acids which fused at 104° F. The yellow matter may be extracted by alcohol from the fat-freed mass; it gives to the alcohol its colour, and is of a bitter taste and unascertained composition. Its aqueous solution is precipitable by acetate of lead and chloride of tin. Ear wax also contains a matter insoluble in ether, alcohol, and water, and this, next to the fat, is its largest constituent; it may be albuminous in nature. Lactate of calcium is said to exist also in this secretion, but no chlorides or phosphates are present.

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[1] *Chemical Physiology*, p. 43.

CHAPTER XVII.

OTHER FLUIDS OF ANIMAL ORIGIN.

Milk.

Milk is the name given to the fluid secreted by the mammary gland of *mammalia*, and is of special interest from the fact that it serves as sole nutriment to the young mammal. It has a bluish white appearance and a specific gravity ranging from 1018 to 1045. When fresh it is of alkaline reaction.

Milk really consists of a clear fluid, in which float a large number of globules of a diameter ranging between 0·0012 and 0·003 inch. These globules contain fat and are enveloped in a thin membrane of caseous or albuminous structure, so that milk does not give up its fat to ether, unless the membrane of the globules is first broken by treatment with acetic acid or potash. It yields about 10 per cent. solid residue and from 0·1 to 0·5 per cent. ash.

When allowed to stand, the fatty portion rises to the top, forming 'cream;' and it may be incidentally mentioned that churning has for its object the mechanical breaking up of the little sacculi to which allusion has been made above.

Milk contains a peculiar kind of sugar termed milk sugar, which under certain conditions of fermentation (at 40° C) is in part resolved into lactic acid, and the rest into grape sugar, which in its turn becomes converted into alcohol. *Koumis*—a fermented liquid consumed by the Tartars—is made by this process.

Milk also contains casein (a form of albumin containing alkalies in combination) and various salts including chlorides of sodium and potassium, phosphates of the alkalies, phosphates of calcium and magnesium, and a quantity of ferric oxide, amounting, according to Haidlen, to about 0·47 per cent. of the ash of milk.

Milk contains from—

2 to 4 per cent. casein
1·5 „ 4 „ fat
4 „ 5 „ lactose

That from woman contains about 0·2 per cent. salts, and that from cows about 0·7 per cent. salts.

But the composition of milk varies somewhat according to the animal, the period of lactation, the food, and so forth.

The following table exhibiting the composition of different kinds of milk is taken from Miller's 'Chemistry :'[1]—

Constituents.	Woman	Cow	Goat	Ass	Sheep	Bitch
Water . . .	88·6	87·4	82·0	90·5	85·6	66·3
Butter . . .	2·6	4·0	4·5	1·4	4·5	14·8
Sugar and soluble salts . . .	4·9	5·0	4·5	6·4	4·2	2·9
Casein and insoluble salts . . .	3·9	3·6	9·0	1·7	5·7	16·0
Specific gravity varies from . . .	1·03	1·03	1·036	1·023	1·035	1·033
to . . .	1·034	1·035		1·035	1·041	1·036

Milk is not coagulated at 100°, although at this temperature a pellicle of casein in combination with some salts, forms on the surface. It is coagulated by mineral and other acids, and the casein may be precipitated out by means of a solution of chloride of calcium.

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[1] Vol. iii. (third edition).

Colostrum is the milk which is first produced after birth of the young animal. It has a yellowish colour, and contains granular bodies consisting of irregular aggregations of small fat globules united by an albuminous substance. The quantity of albumin in the colostrum of the cow is so considerable that it coagulates when heated.

Colostrum is denser than ordinary milk, its specific gravity varying from 1045 to 1050, and approaches serum in quality; in fact, as regards its chemical composition it may be viewed as ordinary milk concentrated to a considerable extent.

The properties of lactose are described in another chapter.

Seminal Fluid.

The seminal fluid is the secretion of the testicles, and constitutes a thick, milky, glutinous liquid of a peculiar odour and of alkaline reaction. It consists of a clear fluid, containing in suspension a number of minute molecules known as *spermatozoa* or *seminal animalcules*. These formations occur in the seminal fluid of all animals, but differ somewhat in form; in man, they assume an elliptical shape, and are also associated with other granular corpuscles of a rounded appearance. The *spermatozoa* possess a curious kind of spontaneous motion, which becomes lost on treatment with various chemical reagents. They are soluble in strong alkaline carbonates.

Before emission, semen is mixed with the secretion of the prostate and Cowper's glands, and hence the natural difficulty of obtaining it for chemical examination is rendered still greater. A quantity, however, may be collected by extracting the tubuli seminiferi from the testicles of animals in the rutting season and squeezing out the contents.

As thus obtained it contains about 86 per cent. water and 14 per cent. of solids. Of the nature of these solids but little, unfortunately, is known, and it is impossible to judge how far chemistry may be concerned in the reciprocal changes that occur in this fluid and the ovum to be fructified during impregnation.

Nevertheless, its chemical composition has been ascertained in some measure. When allowed to stand it becomes clear and is then soluble in water, or almost entirely so, whereas when recently discharged, water seems to have a coagulating effect upon it (in some respects like that of alcohol).

Seminal fluid contains a certain amount of albuminous principles, together with some extractive matters, fat, and salts. Among the organic matters phosphorised principles occur. In short, semen appears to be a kind of organised matter containing the first seeds of all that is essential, when aided by a selective power and a proper medium, to develope into a living creature. Hence it is to be regretted that its chemical composition is known with so little precision.

Mucus.

All the internal parts and cavities of the body which communicate with the external surface, such as the alimentary canal, are lined with what is called *mucous membrane*, and this is kept moist by a fluid termed mucus.

Mucus is a more or less tenacious fluid, of a semi-transparent glairy appearance; it swells up in water, but is not dissolved thereby.

The fluid differs in many of its characters according to the part of the body which yields it.

The substance which gives to it the glairy appearance alluded to is mucin, a form of albuminous matter free from sulphur and very much like 'pyin' in its properties, excepting that it is soluble in excess of acetic acid. Mucin is precipitated from its solutions by alcohol, and by dilute acids (not in excess), but it is not precipitated by heat, tannin, mercuric chloride, or lead acetate.

Mucus contains corpuscular elements which, under favourable conditions, may be seen to transform themselves into epithelium cells, a number of which are generally contained in the fluid.

Mucus also contains small quantities of fat and extractives, the chlorides and lactates of potassium and sodium, a little carbonate of sodium, and a trace of phosphate of calcium.

Nasal mucus contains much chlorides of the alkalies, and the phosphates of the alkalies are also present.

The following analysis of nasal mucus is due to Berzelius:—

Water	933·7
Mucin	53·3
Alcohol-extract and alkaline lactates	3·0
Chlorides of the alkalies	5·6
Water extract + trace of soluble albumin and phosphates	3·5
Sodium combined with mucus	3·9

Nasal mucus, bronchial and pulmonary mucus, mucus from the intestinal canal, gall bladder, urinary bladder,

&c., all present certain differences, while the main characters are identical.

It has its morbid states, and when purulent is like pus in many respects.

Liquor Amnii.

This secretion of the female generative organs, or fluid of the mammalian ovum, surrounds the fœtus. It is clear, colourless, of an alkaline reaction, and has a specific gravity of about 1005. The solid constituents are less than 2 or 3 per cent., and among these are albuminous matters, sugar, urea, lactic acid (?), sodium chloride, magnesium phosphate, and other salts, including sulphate and phosphate of calcium. Some observers also state they have observed the presence of fatty and extractive principles.

Allantoic Fluid.

The allantoic fluid is characterised by the presence of a peculiar ingredient—allantoin, which is a derivative of uric acid, and may be prepared therefrom artificially.

Allantoin, $C_4H_6NO_3$, crystallises in glassy prisms and is soluble in water. By treating uric acid with a dilute solution of acetic acid and addition of peroxide of lead, allantoin is formed and may be crystallised out from the solution.

Synovia.

The origin of synovia is not ascertained, but its purpose seems to consist in the lubrication of the cartilage surfaces of joints. It contains about 94 per cent. water, 3·5 per cent. albumin, 0·5 per cent. of mucin, and 1 per cent. ash. It is of alkaline reaction, and from its diluted aqueous solution the albumin may be precipitated by means of acetic acid.

In the disease called hydrarthon, a great excess of synovia collects in the joints.

The Tears.

The *glandulæ lachrymales* secrete a thin liquid which serves the purpose of preserving the cornea of the eyes in a moist state. When pungent vapours irritate the conjunctiva, or when painful or pleasurable emotions arise in the mind, 'the lachrymal gland exceeds the drainage power of the lachrymal duct, and the fluid accumulating between the lids at length overflows in the shape of tears' (Huxley). So the poet who exclaims, 'Tears, idle tears, I know not whence they come,' is but imperfectly acquainted with the subject!

The tears consist of water containing a few particles of pavement epithelium and a few mucous corpuscles. They are of alkaline reaction and have a saline taste, but the total solid constituents amount to only 1 per cent., and these are chiefly common salt and a yellowish extractive matter which seems to be of similar nature to the aqueous humour.

Of the secretion of the meibomian glands, or gummy secretion of the eyes as it is called, we have no knowledge.

Pus.

Pus is a pathological fluid, and may be produced by violent irritation of the mucous membrane. Simon points out that irritation of a mild character only produces an increase in the secretion of mucus, while an increased excitation causes suppuration and consequent production of pus.

This fluid also forms in other and distinct parts of the body, after pre-existing inflammation and congestion, and to some extent its composition differs with the seat of formation and other conditions.

Pus consists of two parts, a kind of serum or 'liquor puris,' and corpuscular elements resembling the white corpuscles of blood, and almost indistinguishable from mucus corpuscles. When pus, however, is treated with ammonia it is said to become very tenacious and jelly-like, while mucus exhibits this character in a less degree.

The corpuscles of pus are larger than those of blood, and consist of a granular cell-membrane enclosing granular matter in a viscid liquid, and containing a nucleus adhering to the membrane.

The corpuscles by suitable treatment yield myosin (an albuminous principle present in striated muscular tissue). They also yield another albuminous substance termed 'pyin,' but whether it has a real peculiar individuality seems doubtful. It may be obtained by shaking the corpuscles with a 10 per cent. solution of common salt, which dissolves out the myosin (this is precipitated from the salt solution by much water). The insoluble part is then digested with dilute hydrochloric acid, filtered, and the filtrate exactly neutralised with soda, when 'pyin' is precipitated. In fact, 'pyin' seems to be identical with the so-called 'nuclein,' to which allusion has been made elsewhere.

Pyin is precipitated from alkaline solutions by acetic acid, and is not dissolved by an excess of the precipitant.

On the other hand, if hydrochloric acid be used, it is redissolved by an excess. From the hydrochloric solution it is not precipitated by potassic ferrocyanide.

The 'liquor puris' seems to contain a variety of albuminous matters, the chief ones being paraglobulin, casein, and seralbumin. (See Chapter on Blood Chemistry.)

Pus has generally a feeble alkaline reaction, but is sometimes acid and at other times neutral. The solid matters contained in pus amount altogether to about 10 or 15 per cent., and its ash, which contains about 72 per cent. of sodium chloride, is almost identical in composition with that of blood, except that it contains more potassium.

It contains a phosphorised organic principle attached to the corpuscles, and this is perhaps identical with that contained in blood corpuscles. During decomposition the presence of palmitic, stearic, and oleic acids is observed, and these no doubt result from a splitting up of the phosphorised principle above alluded to. (See Brain Chemistry.) These phosphorised principles are easily resolved into their proximate nuclei by a process of hydration, and such a process inevitably occurs when they are allowed to stand in the presence of changing albuminous matters and in contact with water. Pus also contains cholesterine.

Again, decomposing pus yields volatile fatty acids, while the healthy fluid is free from them. They are doubtless products of oxidation of the albuminous matters, or, in other words, products of putrefaction. Similarly, the presence of leucine, tyrosine, xanthine, urea, and uric acid, &c., may be also accounted for. That is to say, 'putrefaction' is the expression by which we indicate a number of changes in progress in organic matters; changes which are in the first place of a character induced by the fixation of the elements of water, and ultimately of a character resulting from the addition of oxygen. These changes are initially due to such microscopic forms of life as bacteria. (See Chapter on Putrefaction, &c.)

These considerations make this a fit place for the mention of the antiseptic treatment of wounds now so much in vogue. It is known that if pus in a state of decomposition be allowed to be absorbed into the lymph or blood it sets up acute pathological processes, such as septicæmia and pyæmia, which sometimes end fatally. The antiseptic treatment of wounds aims at preventing such catastrophes by preventing the decomposition of the pus by the proper applications of certain reagents which either kill the germs which cause the initial changes in pus, or else render them inactive. No doubt, the good results arising from this treatment are in great part due to mere cleanliness, for if the pus be washed off before it has time to decompose, similarly satisfactory results are attained.

In cases of jaundice, pus sometimes contains biliary acids and colouring matters, while in diabetes it sometimes contains sugar.

'Blue pus' derives its colour (so it is said) from a kind of vibrio which yields its pigment to chloroform. This colouring matter is crystalline and is named 'pyocyanine,' but whether it is really derived from the alleged source is by no means clearly established.

In the pus from abscesses, cases of phosphorus poisoning and ulcerated cancers, there is contained a substance which gives a rose-coloured reaction with chlorine water, and is termed chlorrhodinic acid. According to Thudichum, the same substance is yielded by decomposed extract of pancreas and lymphatic glands.

PART V.

CHEMICAL AND PHILOSOPHICAL SUBJECTS

CHAPTER XVIII.

ALBUMINOUS PRINCIPLES, INCLUDING PEPSIN AND PEPTONES.

THE class of substances known in chemistry as albuminous, embraces a very extensive number of bodies, which while they have certain properties common to the whole number, yet present certain distinctions one from the others. They all contain carbon, hydrogen, nitrogen, and oxygen, and some of them also contain sulphur, but this is not an invariable constituent. It has often been stated that some of them contain phosphorus, but this is not correct; wherever phosphorus is present it arises from contamination with phosphates or some such organic combination as lecithine. For instance, F. Miescher[1] has described a constituent of the nuclei of pus-cells as a peculiar albuminous body rich in phosphorus; further papers in reference to the same substance obtained from other different sources have been published by Lubavin,[2] Dr. P. Plosz,[3] Hoppe-Seyler,[4] R. von Jaksch,[5] and by Dr. Miescher,[6] who claims its discovery.

We here reproduce the percentage composition of nuclein, as given by the several authors:—

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[1] *Jahresbericht der Thier-chemie für* 1874 (Maly), being abstract of paper from Hoppe-Seyler's *Med. Chem. Untersuchungen*, 1871.

[2] *Jahresbericht der Thier-chemie für* 1874 (Maly), p. 337.

[3] *Ibid.*

[4] *Ibid.*

[5] Pflüger's *Archiv.* vol. xiii. p. 469.

[6] *Jahresbericht der Thier-chemie für* 1874 (Maly), 337.

[illegible]	[illegible]	From Milk-casein, by Lubavin	From Pus-cells, by Hoppe-Seyler	[illegible]	[illegible]	
[illegible]	[illegible]	48·50	49·58	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	7·15	7·10	[illegible]	7·40	[illegible]
[illegible]	[illegible]	13·30	15·02	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4·60	2·28	[illegible]	[illegible]	[illegible]
[illegible]	—	26·45	—	[illegible]	—	—
[illegible]	—	—	—	—	—	—

[illegible] and Hake have in a recent paper[1] sub- [illegible] published papers regarding so-called [illegible] critical examination. They show that the [illegible] hydrogen, nitrogen, and sulphur (where it [illegible] 'nuclein,' are precisely those which belong to [illegible] and not unlikely impure forms of albumin. The [illegible] ranges in the above quoted analyses from [illegible] per cent., while the carbon ranges between [illegible] per cent.! The absence of sulphur in [illegible] preparations is readily explained by the fact [illegible] treated their preparations with caustic al- [illegible] would remove the sulphur from many forms [illegible] The phosphorus occurring in all cases proves [illegible] of all the preparations, and Kingzett and [illegible] that lecithine (containing phosphorus) is [illegible] constituent of each of the matters from [illegible] been derived, but that the methods [illegible] preparation of this substance would leave [illegible] the phosphorised principle in question. [illegible] also shown by others, that 'nuclein' [illegible] albuminous substance.

[illegible] is usually regarded as the stan- [illegible] substances; other albuminoids being classed according to the degree in which their properties are like or unlike to those of this substance. Thus we have the albumin of serum (seralbumin), and the other modified principles accompanying it in the blood, as well as those which form the solid substance of most of the animal organs and tissues, including those of a bony, cartilaginous, elastic, fibrous, cellular, horny, and epidermic character. Again, there are the various albuminous matters constituting much of the solid parts of plants, and entering into the composition of their juices, and finally, those modified principles derived from albumin and albuminous in character, viz. pepsin and peptones.

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[1] [illegible] Science (Crookes), January 1877.

Albuminous matters seem to depend upon plant life for their synthetical production, although the steps by which they are ultimately formed must be many and complicated: of their nature we have but little knowledge. The herbivora derive them from vegetables in which they are contained, and carnivora from the animal food of which they partake. Thus by such processes of modification as are brought about in the digestive apparatus, these albuminous principles, primarily of vegetable origin, become part of the animal body. So far therefore as albumin is concerned, but only so far, animal life does not embrace a wide synthetical function, but rather one of analysis, for in animal life, albumin is worn down or broken up into simpler products which are eliminated in the excreta. But it has, however, the power of modification and transformation; thus, for instance, the casein of woman's milk becomes ultimately muscular tissue or fibrin, and helps to produce whole series of organs and tissues each and all of which contain albuminous principles of a common origin but different properties.

The principles of which we are treating are often divided into two groups, viz. the albuminoids and the gelatigenous principles, but this is a somewhat arbitrary and needless distinction, for there can be no doubt that both groups are at least referable to a common type. To understand this, it will be well to anticipate a future chapter, and briefly illustrate our meaning by a comparison. The general constitution of any fat may be represented as follows :—

$$C_3H_5 \left\{ \begin{array}{llllllll} HO & \text{substituted} & \text{by} & x & \text{radicle} & \text{of a} & \text{fatty} & \text{acid.} \\ HO & \text{,,} & \text{,,} & y & \text{,,} & \text{,,} & \text{,,} & \text{,,} \\ HO & \text{,,} & \text{,,} & x & \text{,,} & \text{,,} & \text{,,} & \text{,,} \end{array} \right.$$

that is to say, as a tridynamic alcohol, in which the three hydroxyls are substituted by a common radicle or by three different ones. Again, in the brain matter there are found many principles of exceeding complexity, and yet all referable to a common formula, which may be expressed thus :—

$$C_3H_5 \left\{ \begin{array}{lllllll} HO\ .\ .\ .\ .\ .\ . & \text{substituted by} & \text{the residue} & \text{of a} & \text{fatty} & \text{acid} & \text{radicle.} \\ HO\ .\ .\ .\ .\ .\ . & \text{,,} & \text{,,} & \text{,,} & \text{,,} & \text{,,} & \text{,,} \\ HO(OPO)O\ \ OHO & \text{,,} & \text{,,} & \text{,,} & \text{,,} & \text{an amine.} & \end{array} \right.$$

The two primary hydroxyls may be replaced by the residues of palmitic, oleic, stearic, or other fatty acids, while the subsidiary hydroxyl in the larger group (phosphoryl), admits of substitution by the residue of an ammonium base. Thus all compounds of the kind under consideration, may be viewed as basic derivatives of conjugated glycerophosphoric and fatty acids, and while the above formula includes and represents all possible derivatives, it particularises no one individual. No matter what be the nature of the two fatty acids to be obtained, or the nature of the ammonium base resulting on decomposition, they all give glycerophosphoric acid, fatty acids, and a base. In other words, among the products of their decomposition there is one certain constant—viz. phosphoglyceric acid, and with it the other radicles may enter into combination without respect to their individual nature; they have, however, a form in common.

In like manner, when more shall be known of the decomposition products of those substances more particularly here the subject of our study—the albuminoids—it will then be possible to classify them all by one general formula. At present they are classified in the crudest manner, namely in accordance with their simplest properties, or those most readily perceived; but in the future they must be classified according to the constants presented in their decomposition brought about by processes which are calculated to split them up, not into ultimate constituents but into proximate nuclei, or those groups which it may be supposed in their combined arrangement constitute the whole larger conjugated molecules of the primary substance.

Already, chemists have made progress in this direction, and that progress we must now study, merely premising, for the moment, a common constitution to the albuminoids.

The processes of decomposition best destined to lead to the most profitable results in the first place, are those which have been applied so successfully in the study of fats, and those phosphorised principles of brain matter to which reference has been made. These processes all perform a like function—one of hydration—and it is of secondary importance whether for this purpose we use dilute acids or alkalies, or even water at high temperatures or under pressure.

It has long been known that when the white of eggs is boiled for some hours with dilute sulphuric acid or baryta water, it is decomposed, yielding, among other products, ammonia, a volatile sulphur compound (again resolvable into sulphur and sulphuretted hydrogen on treatment with acids), oxyphenol, amido-propionic acid or tyrosine ($C_9H_{11}NO_3$),[1] and amido-caproic acid or leucine ($C_6H_{13}NO_2$),[2] &c.

Braconnot in 1820 also showed that when gelatine is subjected to this process it yields amido-acetic acid, or glycocine ($C_2H_5NO_2$).

Erlenmeyer and Schaeffer found that most albuminoid substances give tyrosine and leucine. Thus working with fibrin, albumin, and syntonin, they obtained for 100 parts of dry matter—

Fibrin . . .	14 parts of leucine,	and 0·8 tyrosine
Albumin . . .	10 " "	" 1·0 "
Syntonin . . .	18 " "	" 8·0 "

Coaglutin yields glutamic acid of the formula $C_5H_9NO_4$, while legumin yields legumic acid, $C_8H_{14}N_2O_2$; but of this last-named product there is some doubt; Ritthausen now regards it as a mixture of glutamic and aspartic acids. Glutamic acid is $C_5H_7(NH_2)O_4$. Hlasiwetz and Habermann have found[3] that most vegetable and animal proteids give aspartic and glutamic acids by boiling with dilute mineral acids, such as hydrochloric acid, and decomposition of the products with oxide of silver.

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[1] Liebig.

[2] Braconnot.

[3] *Chem. Centr.* 1872, p. 535.

O. Nasse[1] has determined the nitrogen given off as ammonia when albuminoids are boiled with baryta water, and has arrived at the following results:—Casein 17 per cent. of its total nitrogen; seralbumin 19 per cent.; fibrin 20 per cent.; glutin 30 per cent.; gelatin 10 per cent.

In later papers[2] the same author gives reasons, based upon experimental data, for believing that syntonins (produced by the action of acids upon albuminoids) are merely partially decomposed products of albumins. Upon continued treatment with hydrochloric acid they yield ammonic chloride, leucine, tyrosine, glucocine, and (as shown by Hlasiwetz) glutamic acid. It should be mentioned that Nasse determined the total nitrogen contained in albuminoids by means of combustion with soda lime, but some chemists do not accept this method as trustworthy. O. Nasse concludes that one part of the nitrogen present in these substances is in combination in a form similar to urea, and that another part is present like the nitrogen in kreatinine, uric acid, &c.

In some earlier papers,[3] P. Schützenberger has shown that when albumin is boiled with dilute sulphuric acid for a few hours it gives two kinds of syntonin, one of which he names hemiprotein, and which is left as an undissolved flaky substance; the other he terms hemialbumin, which is held in solution along with some decomposition products resembling sarkine.

Schützenberger has, however, more especially studied the action of baryta upon albuminoids in the presence of water, and contained in sealed tubes heated to temperatures ranging from 140° to 200° C. By the use of different temperatures, or by stopping the action at different times, various crystallisable and other bodies are observed among the products, but if the action be continued up to a certain point, there is an uniformity in the results.

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[1] *Chem. Centr.* 1872, p. 721.

[2] Pflüger's *Archiv.* vi. 589–616; and vii. 139–155.

[3] *Bull. Soc. Chim.* (2) xxiii. 161–173.

Schützenberger has published many papers upon this subject, and below we give the references[1] to these, while here it will be best to present a summary of his results. One of the most important among these is his confirmation of Nasse's opinion regarding the urea-like combination present in albuminoids. He has not isolated urea, but he has shown that carbonic acid and ammonia are obtained in the proportions which signify that they may be derived from urea, for this substance is split up by baryta into these products. Traces of sulphurous anhydride, sulphuretted hydrogen, oxalic and acetic acids are also found, and 2 or 3 per cent. of tyrosin. Besides these substances there are observed the amido-acids of the series, $C_nH_{2n+1}NO_2$, from amido-œnanthylic acid ($C_7H_{15}NO_2$), to amido-propionic acid; 24 to 26 per cent. leucine ($C_6H_{13}NO_2$); butalanine ($C_5H_{11}NO_2$), and amido-butyric acid; one or two acids allied to aspartic and glutamic acids ($C_5H_9NO_4$ and $C_4H_7NO_4$) and some acids analogous and similar to the legumic acid ($C_8H_{14}N_2O_6$) of Ritthausen; also a small quantity of dextrin-like substance.

Among the new products recently described by Schützenberger is a substance termed by him tyroleucin,

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[1] *Bull. Soc. Chim.* February 15, March 5, and March 15, 1875; *Ibid.* September 1875 (2) xxiv. 145–160; *Compt. Rend.* lxxx. 232–236; *Ibid.* lxxxi. 1108 and 1191; *Ibid.* lxxxiv. 124–126. See also his work on Fermentation.

$C_7H_{11}NO_2$, which fuses at 250°. He represents some of its decompositions as follows :—

$$C_7H_{11}NO_2 = H_2O + C_7H_9NO$$
$$2C_7H_{11}NO_2 = CO_2 + C_8H_{11}N + C_5H_{11}NO_2 \text{ (butalanine).}$$

The body $C_8H_{11}N$ gives a crystalline salt of the formula $2(C_8H_{11}N)2HCl,PtCl_4$.

Schützenberger has represented the early phase of the decomposition of albuminoids thus :—

$$(a)\ C_{72}H_{112}N_{18}O_{22}S + 14H_2O = 2CON_2H_4 + C_2H_4O_2 + S + C_{64}H_{128}N_{14}O_{32};$$

or,

$$(b)\ C_{72}H_{112}N_{18}O_{22}S + 15H_2O = CON_2H_4 + C\ {}_2O_2N_2H_4 + C_2H_4O_2 + S + C_{67}H_{130}N_{14}O_{32};$$

or,

$$(c)\ C_{72}H_{114}N_{18}O_{22}S + 18H_2O = CO_2 + 4NH_3 + C_2H_2O_4 + C_2H_4O_2 + S + C_{67}H_{132}N_{14}O_{32}.$$

He speaks of the C_{67} body as the 'amidated mixture,' and regards it as having been formed by the action of water in the proportion of one molecule for each atom of nitrogen present in the original albuminoid. Of this substance 25 per cent. is constituted of leucine ($C_6H_{13}NO_2$) and leuceine ($C_6H_{11}NO_2$), and he represents its ultimate analysis as follows :—

$$C_{67}H_{132}N_{14}O_{32} = C_5H_9NO_4 + C_4H_7NO_4 + 3C_6H_{12}NO_2 + 4C_5H_{10}NO_2 + 5C_4H_8NO_2.$$

In a study of fibroin from silk, Schützenberger concludes that it differs from ordinary albumin (1) by the nearly total absence of acids of the series $C_nH_{2n-1}NO_4$ from the products of its hydration, (2) by a far smaller proportion of amido-acids of the acrylic series, and (3) by the fact that the amido-acids of the series $C_nH_{2n+1}NO_2$, constituting its principal mass, are the inferior homologues of those predominating in albuminoids. He also concludes that the composition of sericin is not very far removed from that of fibroin.

It cannot be denied that in Schützenberger's papers theory is so mixed with facts that his conclusions can only be generally accepted, while the details (at least in many respects) call for further elucidation. It will yet be seen that modern researches have at any rate given some considerable support to Strecker's view of the albuminoids which supposes them to be composed of a great number of radicles, but that each variety contains one or more such radicles peculiar to itself.

The derivation of amido-acids from albumin and the knowledge of the tendency exhibited by these acids to combine with cyanogen, led Oscar Loew[1] to make some experiments with the view of ascertaining with how much cyanogen, albumin itself would combine, taking Lieberkühn's formula $C_{72}H_{112}N_{18}SO_{22}$ as representing the last-named substance. The experiments were conducted by leading different quantities of cyanogen gas through different solutions of albumin, analysing the sediments which were thrown down after some standing, and those produced by subsequent addition of acetic acid. Among other substances thus obtained, Loew obtained the following :—

$C_{74}H_{118}N_{20}SO_{25}$, or albumin + one molecule of cyanogen and three of water.

$C_{76}H_{128}N_{22}SO_{30}$, or albumin + two molecules of cyanogen and eight of water.

$C_{80}H_{144}N_{26}SO_{38}$, or albumin + four molecules of cyanogen and sixteen of water.

He also obtained other substances from the mother liquors, which appear to be cleavage or decomposition products.

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[1] *J. prac. Chem.* (2) xvi. 60–77.

Berthelot[1] considered that albuminoid substances were complex amides formed by the union of amido-acids of the series $C_nH_{2n+1}NO_2$ (such as glycocine), of tyrosine, certain oxygenated principles, together with some of the acetic and some of the benzoic series; he further considered that chitin, chondrin, &c., contained in addition the elements of glucose. The latest researches, and particularly those of Schützenberger, show that albuminoids are formed by the association in different proportions, of urea and amido-acid combinations belonging, some to the leucine series ($C_nH_{2n+1}NO_2$), some to the aspartic acid series ($C_nH_{2n-1}NO_4$), and others to the benzoic series (such as tyrosine); it is from tyrosine that benzoic and paroxybenzoic acids and bromanil are derived under certain conditions.

It may here be noted that in some chemolytic experiments upon albumin, Thudichum obtained an alkaloid represented by the empirical formula $C_3H_6NO_5$.

Both Guckelberger[2] and Schliesser[3] have investigated the action of oxidising agents upon albuminoids, and it has been shown that the products may be arranged pretty well under the acetic, benzoic, and cyanic series. By acting with a mixture of potassic dichromate or manganic dioxide and sulphuric acid, Guckelberger obtained the following products, and others not so well identified:—

Formic acid
Acetic „
Propionic „
Butyric „
Valeric „
Caproic „

Acetic aldehyde
Propionic „
Butyric „

Benzoic acid
Benzoyl aldehyde
—
Hydrocyanic acid
Valeronitrile

The relative amounts of the different products vary with the nature of the material submitted to oxidation, and to a certain extent they are of a secondary character, leucine, tyrosine, and such bodies being observed only in earlier stages of the reactions. These results agree with those obtained by hydration, and M. Béchamp actually noticed among the products (when potassic permanganate was employed as the oxidising agent) a small amount of urea, and although this was subsequently controverted, yet Ritter as well as Schützenberger have confirmed the fact.

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[1] See his Treatise on Chemistry, 1872.

[2] Liebig's *Annal.* lxiv. 39.

[3] Ibid. lix. 1.

Again, those substances which are obtained when albuminoids are acted upon by the melted alkalies may be regarded as derived from a more energetic action exerted upon the compounds to which baryta water gives rise. So far as determined, they include ammonia, hydrogen, methylamine, aniline, picoline, petinine, leucine, tyrosine, glycocine, carbon-dioxide, and formic, valerianic, butyric, and oxalic acids. In life, albuminoids are subjected to a mixed process of oxidation and hydration, and a study of the results obtained by acting upon these substances with air or oxygen and baryta at the same time, or with peroxide of hydrogen and baryta water in excess, would probably afford peculiarly interesting results.

W. Knop[1] has described a derivative obtained by the action of bromine upon albuminoids, and to which he assigns the formula $C_{15}H_{27}Br_2N_3O_8$, representing its constitution as

$$\left.\begin{array}{ll} \text{Water . . } & H_2O \\ \text{Ammonia . . } & H_3N \\ \text{Bromoxyleucine . } & C_6H_{12}BrNO_2 + O_2 \\ \text{Bromotyrosine . } & C_9H_{10}BrNO_3 \end{array}\right\} C_{15}H_{27}Br_2N_3O_8.$$

He also describes a zinc salt, $C_{15}H_{27}Br_2N_3Zn_2O_{10}$, and a calcium salt, $C_{15}H_{27}Br_2N_3Ca_4O_{10}$, but from certain considerations he is led to quadruple these formulæ, thus assigning to the sulphur-free albuminoid the simplest expression, $C_{64}H_{100}N_{16}O_{20}$, which offers at least some sort of comparison with Schützenberger's 'amidated residue' described above.

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[1] *Chem. Centr.* 1875, 395-399; 411-415; 426-428.

Knop gives to casein a formula which is one half that of the above substance, but all such formulæ merely represent approximate composition, and certainly do not indicate the size of the molecules.

W. Kühne[1] states that when albumin is distilled with a solution containing eight times its weight of potash, a milky alkaline solution containing crystals is obtained. These crystals seem to be composed of indol, thus giving support to the prior observation of Nencki[2] that indol is obtained when albumin undergoes putrefactive change.

M. Nencki,[3] yet later, states that when commercial albumin is digested with finely divided ox pancreas at 40–45° C. in the presence of water for about 70 hours, a body resembling indol is obtained. It melts at about 52°, and gives a nitroso-derivative of the formula $C_8H_6(NO)N$.

When albuminoids undergo putrefaction, they decompose and give rise to products which may be regarded as produced partly by hydration and partly by oxidation; but Liebig went further than this and expressed his belief that all ferments such as synaptase, diastase, pepsin, and yeast, were modifications of albumin in peculiar states of change or decay, without regard to the possibility of the changes being of a definite character as with yeast.

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[1] *Deut. Chem. Ges. Ber.* viii. 206–210.

[2] *Ibid.* vii. 1593.

[3] *Ibid.* viii. 336–338.

All albuminoid substances are capable of existing in the soluble and insoluble state, and all are colloidal in nature. Recent experiments go far to show that many albuminoids, at one time supposed to be widely different, are really identical in nature.

It has long been known that three forms of combination are presented by albuminoids; that is to say, there are combinations with acids, combinations with bases, and combinations with salts. Graham showed that the salts, often associated and yet not in combination, could be removed by dialysis. Schmidt, Aronstein, Heynsius, and Winogradoff, have repeated and confirmed the observations of Graham, but have not extended them in this respect.

A. Gautier[1] states that when blood fibrin is dissolved in a solution of common salt, it gives rise to the production of a substance of like solubility and composition to ordinary albumin. Its solution, however, gives no precipitate with sulphate of copper or argentic nitrate, and coagulates at 6°1, whereas white of egg coagulates at 73°. The author, however, claims to have shown in 1869 that egg albumin contains two substances, one of which coagulates at 71–74°, and the other at 60–63°. When the albumin is obtained from fibrin as described, and isolated by coagulation, there is left in solution another body kept soluble by combination with calcic and magnesic phosphates.

There can be no doubt that many salts have a most decided influence upon the properties of albuminoids. Thus F. Soxhlet[2] has confirmed some observations previously made by Rollet, which tend to show that alkali-albuminate solutions are not precipitated by acids in the presence of neutral sodic phosphate, and it is to the presence of this substance in milk that casein, which in many respects resembles alkali-albuminate, is not thus precipitated. Soxhlet demonstrates by quantitative experiments that the albuminate begins to be precipitated at the moment when the neutral phosphate becomes completely converted into acid salt. W. Heintz[1] differs from Soxhlet in some respects, but Isidor Soyka[2] confirms them on the other hand, and contends that acid albumins and alkali albuminates are both derived from a common principle, the difference of their combinations accounting for differences in their properties.

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[1] *Compt. Rend.* lxxix. 227–229.

[2] *Journ. f. prac. Chemie* (2), vi. 1–52.

A. Heynsius[3] concludes that paraglobulin is identical with alkali albuminate, and he has pursued the studies of Heintz and others with comparable results; but H. Haas[4] differs from Heynsius by maintaining the view that albumin is a soluble compound of globulin with earthy phosphates, and favours Schmidt's view that the solubility of albumin is due to such salts.

Ignoring for the time the differences presented by the various albuminoids, we must now return to view them as containing a parent molecule common to all forms, and for this purpose we shall confine our attention for the moment to egg albumin. Its molecular weight has been approximately determined by analyses of the potassic and platino-hydrocyanic combinations, both of which lead to nearly the same number, 1612. Lieberkühn expresses this composition by the formula $C_{72}H_{112}N_{18}SO_{22}$; and while we must not place too much confidence in this formula, yet its acceptance *pro tem.* proves exceedingly serviceable, notably in such researches as those of Schützenberger and in those we must now describe.

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[1] *Journ. f. pract. Chemie* (2) vi. 374–384.

[2] Pflüger's *Archiv.* xii. 347–377.

[3] *Ibid.* ix. 514–552; and xii. 549–596.

[4] *Chem. Centr.* 1876, 795–800; 811–816; 824–832

Towards bases, albumin plays the part of an acid, while towards acids it behaves as a base.

Among other compounds with bases the following ones are the best known, but the same reserve must be exercised in their acceptance as with Lieberkühn's formula for the molecule of free albumin.

Albuminate of barium, $C_{72}H_{110}BaN_{18}SO_{22} + H_2O$ (?), produced by precipitation of an alcoholic solution of potassic albuminate with soluble barium salts.

Albuminate of copper, $C_{72}H_{110}CuN_{18}SO_{22} + H_2O$ (?). According to Lassaigne double compounds of this salt with those of barium, calcium, magnesium, and potassium exist.

Albuminates of lead and mercury are also known.

Albuminate of potassium, $C_{72}H_{110}K_2N_{18}SO_{22} + H_2O$ (?) may be prepared by mixing white of egg with strong potassic hydrate and washing the gelatinous product with water. When freshly prepared it is soluble in alcohol, but loses this property on drying.

Neutral albuminate of sodium, $C_{72}H_{110}Na_2N_{18}SO_{22} + H_2O$ (?), and an acid salt of the composition $C_{72}H_{111}NaHN_{18}SO_{22} + H_2O$ (?) is believed also to exist in blood serum and white of egg.

Albuminate of silver, $C_{72}H_{110}Ag_2N_{18}SO_{22} + H_2O$ (?) and albuminate of zinc, $C_{72}H_{110}Zn_2N_{18}SO_{22} + H_2O$ (?) are both prepared by precipitation of albuminous solutions with appropriate salts.

G. S. Johnson has described[1] what he believes to be definite compounds of albumin with various acids. His general method of preparation consisted in placing white of egg in a hoop dialyser of parchment paper floating upon dilute solutions of the acids. The results he has obtained incidentally confirm the formula assigned by Lieberkühn to albumin, as is seen by the following table :—

	Formula	Acid contained	Acid required by theory.
		Per cent.	Per cent.
Nitrate . .	$C_{72}H_{112}N_{18}SO_{22}.2HNO_3$	6·796 (mean)	7·24
Hydrochloride .	$C_{72}H_{112}N_{18}SO_{22}.2HCl$	3·93	4·33
Sulphate . .	$C_{72}H_{112}N_{18}SO_{22}.H_2SO_4$	5·36	5·73
Orthophosphate.	$2C_{72}H_{112}N_{18}SO_{22}.3H_3PO_4$	8·47	8·35
Metaphosphate .	$C_{72}H_{112}N_{18}SO_{22}.HPO_3$	4·37	4·72
Citrate . .	$C_{72}H_{112}N_{18}SO_{22}.2C_6H_8O_7$	6·54	7·06
Oxalate .	$C_{72}H_{112}N_{18}SO_{22}.H_2C_2O_4$	5·32	5·28
Tartrate . .	$C_{72}H_{112}N_{18}SO_{22}.2H_4C_4O_6$	15·63	15·68
Acetate . .	$2C_{72}H_{112}N_{18}SO_{22}.3C_2H_4O_2$	5·49	5·37

It should be stated, however, that the author of these experiments did not submit his products to complete analysis, but only determined the acids entering into the composition of the different preparations.

The great difference between albuminoids and gelatigenous substances is that the latter contain no sulphur ; this is quite a subservient feature, however, in their constitution, although we do not yet know the nature of the combination by which sulphur enters into the constitution of the albuminoids.

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[1] *Journ. Chem. Soc.* August 1874.

In the following table the approximately identical composition of different albuminous bodies is exhibited :—

	Egg Albumin (Mulder)	Seralbumin (Mulder)	Blood Fibrin (Mulder)	Casein (Mulder)	Globulin (Mulder)	Vitellin (Gobley)	Lardacein	Gelatin	Legumin (Dumas and Cahours)
C.	53 5	53·3	52·7	53·83	54·5	52·26	53·6	50·16	50·53
H.	7·0	7·1	6·9	7·15	6·9	7·25	7·0	6·60	6·91
N.	15·5	15·7	15·4	15·65	16·5	15·06	15·0	18·30	18·15
S.	1 6	1·3	1·2	0·85	22·1	1·17	1·3	0·14	24·41
O.	22·0	22·6	23·5	22·52		23·24	23·1	24·80	

It is unnecessary to enumerate the results of further analyses by many authors, otherwise there would be no difficulty in doing so. They all prove that, arranged under the title of albuminous matters, there are hundreds of substances nearly allied and yet not identical ; having many properties in common and some distinctive ones; having all the same general constitution, but differing more or less in the nature of the smaller radicles composing the larger proximate nuclei.

The principles less rich in carbon, but richer in nitrogen, are generally viewed as entering into the composition of the less vital tissues, such as bone-cartilage, tendons, connective tissue, and skin. When these are boiled for a long time with water, they yield solutions which gelatinise on cooling. Non-hardening cartilages yield a like substance termed chondrin.

	C.	H.	N.	O.
Gelatin	50·0	6·6	18·3	25·1
Chondrin	49·1	7·1	14·4	29·4
Ossein	50·4	6·5	16·9	26·2

Isinglass is another form of gelatin, while silk gelatin, or sericin $C_{15}H_{25}N_5O_8$ (?), and fibroin of silk, $C_{15}H_{23}N_3O_6$(?), (forming its chief constituent), have many properties in common with other gelatigenous principles. These principles appear to be free from sulphur, and on decomposition with acids or baryta water yield products characteristic of albuminoids.

General Properties of the Albuminoids.—These principles may be preserved in a dry state for an indefinite period without suffering decomposition; but in the presence of air and water, they readily putrefy, and among the products of their change we find carbonate, butyrate, valerate, and sulphide of ammonium, leucine, and tyrosine.

They have a sp. gr. ranging from 1·2 to 1·4. Thus W. Dittmar[1] has determined that of legumin at 1·285–1·36, and glutin at 1·297.

As isolated from their different sources they are often associated (in combination) with bases or salts, particularly phosphate of calcium, which is left in the ash when they are incinerated.

When heated in close vessels they swell up, blacken, give off sulphuretted hydrogen, ammonia, and fœtid empyreumatic products, leaving a porous carbonaceous residue.

As they exist in living plants and animals, they are in combination with water of colloidation to a greater or less extent; that is to say, the water is combined in a manner parallel to that in which it exists in crystals. This water cannot be separated, as from a sponge, by pressure.

Most or all albuminoids can exist in the two states, soluble and insoluble, in water. When gently heated with dilute solutions of potash or soda, they easily dissolve, and in general the sulphur is removed by the same process and forms sulphide of the base employed. From the alkaline solution, acids precipitate what Mulder termed protein, and which he regarded as the essential principle of all albuminoids; albumin, fibrin, casein, &c. were thus considered by him to be derivatives of protein. It is not worth while to study Mulder's views further: so far as they have been substantiated by more modern work, the information given before has already sufficiently described; it is probable that the protein of Mulder is a kind of syntonin or gelatin. He assigned to it the formula $C_{18}H_{27}N_4O_6,H_2O$, and maintained its freedom from sulphur against a different opinion held by many other chemists.

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[1] *Versuchs-stationen Organ*, xv. 401–403.

When once dried, all forms of the albuminoids are insoluble in alcohol and ether.

Aqueous solutions are coagulated by alcohol and are precipitable by solutions of the salts of copper, lead, and mercury, tannic acid, &c. &c.

This power of combination with tannic acid which is exhibited by the albuminoids and gelatins supplies the chemical explanation of the manufacture of leather.

Concentrated sulphuric acid dissolves the albuminoids with a brownish red colour.

Concentrated nitric acid produces in their solutions a bright orange coagulum which gradually dissolves with effervescence; this coloured substance was termed by Mulder xanthoproteic acid.

Strong hydrochloric acid warmed with albuminoid solutions gives a milky coagulum which dissolves slowly to a blue or violet-coloured solution.

Albuminoid solutions containing acid give with potassic ferro- and ferri-cyanide, precipitates not furnished by ordinary aqueous solutions.

Millon's so-called reaction consists in moistening any suspected tissues with a solution of 2 parts of mercury in 4 of nitric acid (of the sp. gr. 1·40); on warming gently (below 100° C.) an intense red colour is produced if albuminoid matter be present, which is indestructible by boiling with water or on exposure to the air.

Albuminoid solutions possess extremely low diffusive powers and turn the plane of polarised light to the left.

The albuminoids are distinguished from the gelatinous principles by giving precipitates with potassic ferrocyanide; solutions of gelatin are said also to give no precipitates with lead acetate, cupric sulphate, dilute mineral acids and alum.

Notes on Individual Albuminoids.

In Chapter VIII., while treating of the chemical constitution of blood, the various albuminous matters contained in it have been already described. We must, however, recur here to the chief properties of seralbumin, in order to compare it with other allied substances.

Serum albumin, or seralbumin, as it is termed, may be obtained from blood serum by precipitation with lead acetate, washing with water, and decomposition of the precipitate suspended in water by means of carbonic anhydride. A cloudy solution of albumin is obtained on filtration. If this solution be evaporated at a gentle temperature (about 52° C.), it leaves a yellow transparent substance, which is mainly soluble in water, and entirely dissolves when aided by the presence of a little acetic acid. Its aqueous solution is precipitable by alcohol. The continued contact with alcohol renders it coagulated or insoluble. Its specific rotation for yellow light is −56°. It is not precipitated by small quantities of very dilute acids, but in greater quantity, acids (particularly nitric acid) precipitate it, as do also carbolic acid, mercuric chloride, potassic ferrocyanide, lead acetate, and argentic nitrate. Its solution coagulates at 73° C.

When contained in caustic alkaline solutions, it is not completely coagulated by heat until the solution be exactly neutralised.

As isolated by the method described, or by adding acetic acid to blood serum, filtration from other albuminoid matters thus precipitated, and also by carbonic anhydride, and dialysis of the filtrate of seralbumin to free it as far as possible from salts, it yet still contains some saline matter, and the point of coagulation is dependent partly upon the nature and quantity of this.

Albumin from White of Eggs, or Ovalbumin, presents some similar characters to seralbumin. Its specific rotatory power for yellow light is −35·5°, and unlike seralbumin, it is coagulated by ether.

S. Rother states[1] that it is maintained in solution in the presence of starch even at a boiling temperature; a drop of strong nitric acid, however, causes coagulation. Coagulated seralbumin, or ovalbumin, if heated to 300° F. with a small quantity of water, redissolves, and gives a liquid not coagulable by heat, but which, when acetic acid is present, is precipitated by potassic ferrocyanide. Albumin precipitated from solutions by other agencies than boiling, such, for instance, as those exercised by certain salts, is not necessarily in the coagulated state; that is to say, it will often dissolve in pure water.

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[1] *Pharm. Journ. Trans.* (3) iii. 644.

Egg albumin, unlike seralbumin, is precipitated by oil of turpentine, and is not easily soluble in strong nitric acid.

Paralbumin is the name which was given by Scherer to a substance he obtained from the fluid of ovarian cysts. It is generally associated with a starch or glycogen-like body capable of change into sugar. Its solution is viscid and precipitable by acetic acid and carbonic anhydride. It is not precipitated by magnesium sulphate, but in other respects resembles ordinary albumin.

Metalbumin is met with in dropsical fluids, and is much like paralbumin. It is not, however, coagulable by heat. Alcohol precipitates it from its solutions.

Para-Globulin may be obtained from blood serum as described; it is said to differ somewhat from ordinary globulin by virtue of its fibrino-plastic properties exhibited in the production of fibrin (as also previously described) when mixed with certain liquids such as hydrocele fluid.

Globulin exists in aqueous humour, in the juice of the cornea, connective tissue, &c. It may be prepared by rubbing up fresh lenses[1] of the eyes of bullocks with pounded glass and water, and precipitation of the filtrate with carbonic anhydride. Alcohol also throws it down from its solution. Acetic acid solutions are precipitated when neutralised with ammonia.

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[1] These contain, according to Simon, from 10 to 14 per cent. globulin.

In its coagulated form it is insoluble in water; but it is soluble in certain neutral saline solutions.

Myosin is the substance which by its separation and coagulation in muscular tissue after death induces 'rigor mortis.' As the myosin decomposes, this condition passes. The substance was first obtained by Kühne.

In order to prepare it, muscular tissue is minced finely and washed with water thoroughly, until the washings are no longer acid and are not precipitated by mercuric chloride. The residual mass is well rubbed up with a 10 per cent. solution of common salt, and the filtered solution is then precipitated by dilution with water; it is purified by re-solution in chloride of sodium and reprecipitation by dilution.

Myosin is insoluble in water, soluble in very dilute hydrochloric acid, and soon passes into the state of syntonin. It is also soluble in dilute alkalies, becoming alkali-albuminate. By heat it is coagulated out of solution; it is also coagulated by alcohol.

Vitellin, an albuminous matter contained in the yolks of eggs, has not been obtained at all pure. So far as this has been effected, it has been shown to be like myosin.

Acid-albumin is the name given to the substance produced by acting on seralbumin or other albuminoids with dilute acids such as hydrochloric. These solutions probably contain the compounds described by Johnson. (See above.) Such solutions may be gradually heated to 70° without coagulating, and even at higher temperatures coagulation may be entirely prevented. The resulting fluid rotates a ray of yellow light 72° to the left.

On neutralisation, insoluble albumin is precipitated, but the precipitate thus obtained dissolves in alkalies.

Alkali-Albumins, or Albuminates.—This class, together with the acid-albumins, is sometimes classified together as *derived* albumins.

Casein is the most important alkali-albuminate, although, as we have had occasion previously to point out, it is possible to produce substances by the action of dilute alkaline solutions upon ordinary forms of albumin which are precipitated by neutralisation, and which cannot be distinguished from casein.

Casein occurs plentifully in the milk of animal feeders, and from this fluid it is readily obtained by precipitation with magnesium sulphate, filtration, and washing with a concentrated solution of salt. By dissolving in pure water it may be separated from any butter which may be present, and it may be further purified by precipitation with acetic acid. After drying, casein swells in water, but will not dissolve except in the presence of free alkali. On neutralising the alkaline solution, the precipitate so obtained is soluble in an excess of acetic or hydrochloric acid.

Alcohol precipitates neutral or feebly alkaline solutions of alkali-albuminate or casein when cold, but the precipitates redissolve on heating.

Casein is coagulated by certain animal membranes, as is witnessed in curd making : the curd results from the action of *rennet* derived from the stomach of the calf.

Plant-casein, or legumin, is found chiefly in the seeds of leguminous fruits, from the juice of which it is precipitable by acetic acid or rennet.

Fibrin, or *Fibrinogen*, has been described under Blood.

Plant fibrin occurs in plants in an insoluble state, especially in the seeds of cereals, and may be obtained from crude gluten by extracting it with dilute alcohol to remove vegetable gelatin (glutin), and afterwards with ether to extract the fat. The residue is impure plant-fibrin. It behaves like ordinary fibrin in its reactions.

Lardacein, a body resembling albumin in its percentage composition and some of its properties, is found deposited in the smaller arteries of certain organs, such as the liver, kidney, spleen, brain, and intestines, when diseases associated with suppuration and cachexia are supposed to exist. It is otherwise known as 'amyloid substance,' from the fact that it strikes with iodine and sulphuric acid a blue coloration. Virchow considers it as an altered fibrinous deposit.

It is found in the spinal marrow and brain, &c., in locomotor ataxia, but it has not yet been sufficiently well isolated to establish its nature.

Gelatin is obtained by boiling connective tissue, tendons, &c. in water: from bones it is best made by dissolving out the earthy matters by means of hydrochloric acid, and boiling the residue with water. It swells up in water and dissolves on boiling, to a viscid liquid which gelatinises on cooling, even if it contains only 1 per cent. When dried, it is insoluble in ether and alcohol.

Solutions of gelatin are precipitated by tannic acid, alcohol, and salts of mercury, but not by alum or by neutral or basic lead acetate, potassic ferrocyanide, dilute mineral acids, &c.

Size and glue are impure forms of gelatin.

Chondrin is obtained from the cartilages of ribs and joints, and is much like gelatin, but differs from it in being precipitated from its aqueous solution by means of alum, acetic acid, lead acetate, &c., but not by mercuric chloride. Boiled with hydrochloric acid, it is said to yield glucose; further investigation might lead to some connection therefore between this body and amyloid substance.

Of Sericin and Fibroin from silk we have already treated (pp. 336 and 337).

Elasticin is the special principle of yellow elastic tissues, such as the middle coats of arteries and veins, &c.

Keratin is obtained in an impure form from horny matters, as horn, feathers, hoofs, epidermis, &c., by extracting other matters first with alcohol and ether.

Mucin is obtained from mucous fluids, &c.

Pyin, which resembles mucin, is obtainable from fresh pus; it is said to give rise to a blue crystalline substance not well known, but termed pyocyanine.

The following table is taken from Fownes' 'Chemistry' (12th edition):—

Solubilities of Albuminoid Principles.

Soluble in water:—
  Aqueous solutions not precipitated by boiling = Peptones.
  " " coagulated " " = Albumins.
Insoluble in water:—
  Soluble in 1 per cent. solution of sodic chloride = Globulins.

Insoluble:—
  Soluble in hydrochloric acid (0·1 per cent.) in the cold.
  Soluble in hot spirit . . . . . . = Alkali-Albumin.

Solubility of Albuminoid Principles—continued.

Insoluble in hot spirit	=	Acid-Albumin.
Insoluble in hydrochloric acid (0·1 per cent.) in the cold:—		
Soluble in hydrochloric acid (0·1 per cent.) at 60°	=	Fibrin.
Insoluble in hydrochloric acid (0·1 per cent.) at 60° Also insoluble in strong acids; soluble in gastric juice	=	Coagulated Albumin.

Pepsin and Peptones as Albuminoids.

Elsewhere (in the Chapter on 'Gastric Digestion') we have referred to the action of so-called pepsin in converting insoluble albuminoids into solutions called peptones. In spite of the great differences observed between the various albuminous compounds, they are all, by the action of the gastric juice or the pancreatic juice, reduced and converted to solutions which exhibit but few distinctive characters, no matter what be the specific substances thus resolved.

The precise part exercised by pepsin is not known; it has certainly been isolated in an imperfect form, but its composition is unknown; it is probably itself of an albuminoid character, but of its constitution we know nothing, and of its history in the process of digestion we have but little information. Of its action there seems to be no doubt, although it is true that the acid of the stomach is of itself capable of resolving albuminoids into more or less soluble and metamorphosed substances.

The change may be best exhibited in the laboratory at the temperature of the blood with any of the dilute mineral acids. Albuminoids thus influenced change first into so-called syntonines or bodies which give less nitrogen as ammonia, when boiled with strong alkalies or baryta water. Syntonins themselves are decomposed, when boiled with acids or strong alkalies, in the manner described by Schützenberger and those other chemists whose researches we have already described.

Whether, therefore, pepsin does more than accelerate the action of dilute acids we cannot say with certainty; if it does, the action is entirely unknown and is likely to remain so as long as men are content to study the question as it has been too often studied heretofore.

It seems to be the object of certain so-called physiological chemists to try the action of pepsin upon albuminoids, in order that when they have obtained the solutions of peptones they may be subjected to a set number of well-known tests. These consist of non-precipitability by boiling, neutralisation, or strong acids, but precipitability by alcohol and by such reagents as sulphate of copper and potassic ferrocyanide. But when it has been shown that precipitates are yielded with tannic acid, argentic nitrate, mercuric chloride, platinic chloride, and plumbic acetate, the measure of their investigative power is satisfied, and they never dream of following up in a logical manner the study of any one of these combinations and by so doing obtain some definite result. 'As it is, however, our literature and our text-books abound with descriptive matter concerning what may appropriately be termed "test-tube chemistry." The test-tube as an agent in pioneering experiments, as a preliminary to the application of elaborated methods of research, based, indeed, in the first instance, upon such reactions, is invaluable; but employed as a final test of character and constitution, these reactions are absolutely without meaning. A precipitate or a colour may result from the mixture of two solutions, but no amount of repetition of such reactions can teach us more than the experience of the fact. To the precipitate we must apply methods of purification and analysis, in order to ascertain its composition, and for the colour we must use the spectroscope, or other means at our command which shall in like manner identify for us its nature. But when we have effected all this we have but begun, for it yet remains to learn the inner constitution of the body whose empirical formula we have established; even then we have yet to determine in what way it was in the first place produced from the mixture. Then, and not till then, are the resources of the chemist exhausted and the problem solved. Now, by some of the reactions above indicated, it will appear reasonable that phospho-molybdic acid would precipitate many peptone solutions, in which case it is not unlikely that by the subjection of the products to decomposition with baryta water, and further treatment of the free substances, some very definite results would be obtained. Meanwhile a general name represents all we know of substances which will one day prove to have a constitution, complicated certainly, but as evident and as well defined as those of the best-known bodies.'[1]

To one of the few attempts which have been made to assign formulæ to the constituents of peptone solutions reference has been already made (pp. 70, 72), but we must now notice it more in detail, more particularly because the attempt has been made, rather than to any great faith that is to be placed in the results.

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[1] *Physiology and its Chemistry, &c.*, by C. T. Kingzett and H. W. Hake. *Quarterly Journ. of Science*, January 1877.

Basil Kistiakowsky, of Kiew,[1] has attempted to determine whether the peptones formed in pancreatic digestion differ in composition from their albuminous sources, and whether they differ one from the other in composition and properties according as different albumins are used; also whether, when from the same albumin, the gastric and pancreatic peptones are identical.

In an experiment with ox fibrin he found on analysis a formula for it as follows—$C_{139}H_{226}N_{37}SO_{46}$, and this was subjected to the action of pancreatic ferment isolated by Wittich's method. To the resulting peptone, obtained after about twelve hours, he assigns the formula $C_{113}H_{228}N_{36}SO_{66}$; that is to say, it differs from the original substance in containing less carbon and more oxygen. Both preparations gave a certain percentage of ash, which may, for the present considerations, be left out from notice. The peptone thus obtained, like others, is of a fluorescent character. A peptone obtained from vegetable casein (from sweet almonds) proved to be of characters and composition almost identical with that from fibrin; as expressed by the analyses its formula was $C_{115}H_{224}N_{36}SO_{65}$.[2]

From analyses of peptones produced by imitative processes of gastric and pancreatic digestion it appears, according to Kistiakowsky, that they differ only slightly; the gastric peptone contains more carbon and oxygen.

Finally, by the action of pancreatic ferment upon fibrin the author obtained leucine, tyrosine, and glutamic acid. S. Radziejewski and E. Salkowski[3] have also observed these products together with aspartic acid as an accompanying substance.

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[1] Pflüger's *Archiv. f. Physiologie*, ix. 438–459.

[2] It is interesting to compare these formulæ with those of albumin, and the various derivatives obtained by Schützenberger and Knop.

[3] *Deut. Chem. Ges. Ber.* vii. 1050–1051.

R. Maly,[1] contrary to the experiences of Kistiakowsky, finds that the peptone prepared from fibrin is almost identical with the original substance, and so also with albumin and its peptone. In short, he contends that a peptone is not a product of the splitting up of its generators, but he does not support his conclusion with any analyses.

A. Kossel[2] is in conflict with R. Maly, and states, contrary to him, that peptones do not give precipitates with acetic acid and potassic ferrocyanide; where such precipitates obtain, they result from contamination of the peptones with unchanged albumin. In fact, A. Kossel confirms Kistiakowsky's statements, and those of Lubavin, to the effect that peptones possess characters common to the amidic acids. To be brief, it may be stated that all we know regarding peptones tends to show that they represent intermediate stages between albuminoids and the products of decomposition obtained by the action of hot acids and alkalies upon these principles. At the same time the change is so slight that in the blood, the synthetical influences they are subject to, are powerful enough to cause the re-formation of albumin or fibrin which is assimilated in the cells of the body to replace those parts chemically destroyed by the acts of life. On such a view alone, is it possible at present to understand the production of fibrin by the coagulation or whipping of blood, and it is one which agrees with Schmidt's explanation of this phenomenon, for as we have already seen, he regards the production of fibrin as resulting from the combination of two principles.

According to Brücke, pepsin occurs not only in the stomach, but also in the blood, the muscles, and the urine, and it is to be confessed that meat introduced into a subcutaneous wound certainly undergoes a sort of digestion (Bretonneau). But however this may be, it is probable that the action of pancreatic and gastric ferments consists like that of acids and dilute alkalies in a process of mild hydration. Of ferments themselves we shall treat more fully hereafter.

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[1] Pflüger's *Archiv. f. Physiologie*, ix. 585–619.

[2] *Ibid.* xiii. 309–320.

Leucine, Tyrosine, &c., as produced by the Decomposition of Albuminoids.

Elsewhere in this work it has been shown that glycocine ($C_2H_5NO_2$) is amido-acetic acid, and that as occurring in the body, it is identical with the product produced from the haloid derivatives of acetic acid by certain double decompositions. Again, hippuric acid has been shown to have a distinct relation with glycocine, and, indeed, splits up, when suitably treated, into benzoic acid and glycocine, from which substances it has also been artificially prepared. Now there can be little doubt that these and other similarly constituted bodies are primarily derived from the decomposition of albuminoids, and in the chapter treating of these, it has been stated that the principal among such products of decomposition are leucine and tyrosine, substances which are also found in nearly all the glandular organs and secretions of the body.

Chemical researches have demonstrated the identity of amido-caproic acid, $C_5H_{10}(NH_2)CO(OH)$ (as obtained by acting upon bromocaproic acid with ammonia), with leucine found in the body and as a product of decomposition of albuminoids. Further, by acting on methylamine, $NH_2(CH_3)$, with chloracetic acid; methylamidoacetic acid, $CH_2(NHCH_3)CO(OH)$, is obtained, and this substance is now known to be identical with sarkosine, which in its turn gives rise to the production of kreatine by direct union with cyanamide (NH_2CN).

So there can be but little doubt that when the products of the decomposition of albuminoids are better known, it will be found that they comprise many similar derivatives referable to acetic acid or its homologues, and indeed this may be considered to be established to some extent even in the case of tyrosine ($C_9H_{11}NO_3$).

H. Ost[1] has recently conducted some researches bearing upon the constitution of tyrosine. When potassium salicylate is heated, paraoxybenzoic acid is produced, and when tyrosine is fused with potash it also gives rise to the formation of this substance (Barth). But inasmuch as when salicylic acid is heated with soda, a salicylate and not paraoxybenzoate is produced, it was doubtful whether tyrosine is really a derivative of salicylic acid or paraoxybenzoic acid. Now paraoxybenzoic acid fused with soda gives rise to a paraoxybenzoate only, and not to salicylate, hence Ost concluded that if tyrosine when fused with soda gives rise to paraoxybenzoic acid, it must be a derivative of that substance, and this he found to be the case, ammonia and hydrogen being evolved when a mixture of the substances was heated upon an oil bath.

Although it will thus be seen that something is known about the constitution of tyrosine, yet its precise constitution is far from established. Some chemists consider it to be oxyphenyl-amidopropionic acid, but on certain other grounds, the presence of an amidogen group is disputed. But that it will prove to bear a general relation to leucine and other bodies accompanying it in its formation, would seem to be certain.

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[1] *Journ. prac. Chem.* (2) xii. 159.

Before passing on to study leucine and tyrosine individually, we may take note of a paper by E. Dreschel[1] bearing upon the oxidation of these substances and glycocine.

He points out that when an ammoniacal solution of glycocine is treated with ammonium permanganate, there is formed a precipitate of peroxide of manganese ; and inasmuch as on addition of calcium nitrate to the filtrate, calcium carbonate and oxalate are precipitated and more of this mixture formed on boiling, he concludes that the solution must have contained oxamic and carbamic acids (amides of oxalic and carbonic acid ; see 'Urea').

The same amides are formed when an aqueous solution of glycocine is oxidised with potassic permanganate and also when leucine, tyrosine, or albumin are similarly treated.

Reasoning on these facts, E. Dreschel concludes that in the formation of urea from albuminoids, these are first resolved (as is known) into glycocine, tyrosine, leucine, &c., and then these latter are converted by the oxygen of the blood into a carbamate which is finally transformed by a ferment into urea.

The author appears to have confirmed his opinion by preparing calcium carbamate $NH_2.(CO.O(CaO)H)$ from the serum of dog's blood.

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[1] *Journ. prac. Chem.* (2) xii. 417–426.

These considerations, when studied with those given under 'Urea' and 'Albuminous Bodies' are specially interesting as elucidating the chemical changes continually going on in the living body.

We may now, without further digression, pass on to the more particular study of leucine and tyrosine.

Preparation of Leucine and Tyrosine.

Leucine is found in the animal economy wherever tyrosine is met with, and particularly is this true of the lung and liver tissue. In urine both substances are only present in cases of deep disease; thus they have been detected in jaundice, in acute yellow atrophy of the liver, small-pox, and typhus, &c. In very bad cases of malignant jaundice, 'the finer branches of the hepatic veins are filled with crystalline granules and firm yellowish grey strings of matter containing crystals in the shape of balls with a radiary arrangement, and bundles and sheaves of needles. The balls are leucine and the needles tyrosine' (Thudichum).

These substances may be readily prepared by the artificial decomposition of every albuminous substance, such as ovalbumin or seralbumin, fibrin, casein, gelatin, muscular tissue, legumin, wool, or horn. Horn shavings form a ready source for their preparation. They are boiled for several hours in about twice their weight of dilute sulphuric acid (containing about 20 per cent. H_2SO_4). The mixture is then treated with an excess of milk of lime and boiled again for another three or four hours, in which operation, ammonia and certain organic ammonia compounds and sulphur are expelled. To the filtered liquid is then added a slight excess of sulphuric acid or acetic acid, filtration resorted to (when the first named acid is used), and the fluid evaporated with a view to concentration. On cooling of the concentrated liquid, crystalline tufts of tyrosine are first deposited, and from the mother liquors, on further concentration, scales of leucine are separated.

Of course there accompany leucine and tyrosine in the primary liquid a number of decomposition products of unascertained nature, although perhaps equally important, together with glutamic and aspartic acids, and those other amido-acids of which a brief description has been given when describing Schützenberger's researches on albuminoids in the chapter on that subject.

Another good source of leucine and tyrosine is the dry residue obtained in the preparation of extract of meat.

Instead of the sulphuric acid in the operation above described, caustic potash or soda may be used, if preferred, in which case the subsequent proceedings have to be adapted to these altered circumstances.

Bopp[1] recommends *fusing* dried casein or other albuminous matters with their own weight of caustic potash; ammonia and (subsequently) hydrogen are evolved, and when the mixture changes colour from dark brown to yellow, the reaction is considered to be completed. The mass is then cooled, and on treatment with water gives a solution which after slight acidification with acetic acid and concentration, deposits first tyrosine and then leucine.

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[1] Liebig's *Annalen*, lxix. 21.

Purification, Properties, and Decompositions of Leucine.

For the purification of leucine Thudichum recommends[1] trituration and gentle heating with concentrated nitric acid until a slight reaction is perceptible. The solution is then diluted with much water and fully precipitated with nitrate of mercury, filtered, and the filtrate allowed to stand for several days. The secondary deposit which forms under these circumstances is separated by filtration and the fluid neutralised by ammonia, then evaporated to the point of crystallisation. The leucine so obtained (in plates) is further purified by recrystallisation from moderately strong boiling alcohol.

When present in urine, leucine separates in oily drops from the concentrated solution, but if these are isolated and dissolved in hot alcohol, the fluid deposits the crystalline substance on cooling.

Thudichum[2] also gives a method of obtaining leucine from all animal fluids. These are fully and successively precipitated with neutral and basic acetate of lead, and the filtrates freed from lead by hydrosulphuric acid, after which they are treated with sulphate of copper until a filtered sample gives with potash a blue precipitate. The mixture is then freed from sulphuric acid by boiling with barium carbonate, and the ultimate clear solution evaporated near to dryness, when a compound of leucine with copper, having the empirical formula $C_{18}H_{35}Cu_2N_3O_6$, is deposited.

Leucine is not unlike cholesterine in appearance, being unctuous to the touch and having a specific gravity less than that of water. By careful heating it may be sublimed unchanged, and in this state it presents a woolly mass which is seen under the microscope to consist of an aggregation of rhombic plates. At a higher temperature (170° C.) it melts, and when still further raised it suffers decomposition, yielding among its products of change a yellow oily liquid containing much carbonate of ammonium and amylamine ($C_5H_{11}(NH_2)$).

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[1] *Pathology of the Urine.* 2nd edit., p. 512.

[2] *Ibid.*

Leucine is soluble in 27 parts of water at normal atmospheric temperatures, its solubility both in water and alcohol being increased by the presence of acetic acid or potassic acetate. It is sparingly soluble in cold absolute alcohol, and insoluble in ether. It dissolves in 658 parts of 75 per cent. alcohol, and in 1040 parts of 96 per cent. alcohol; it is also soluble in alkalies.

When dissolved in the acids it combines therewith, forming crystallisable compounds.

Although the watery solution of leucine is not precipitable by salts of metals with mineral acids, yet when boiled with certain chlorides or acetates, leucine expels the acids and forms insoluble compounds with the metals.

Among the most important compounds are the following:—

Hydrochloride	$C_{16}H_{13}NO_2HCl$
Nitrate	$C_6H_{13}NO_2HNO_3$
Monocupric dileucine	$2(C_6H_{12}NO_2)Cu$
Dicupric trileucine	$2(C_6H_{12}NO_2)Cu,C_6H_{12}CuNO_2$
The mercurial salt	$2(C_6H_{12}NO_2)Hg$
The lead salt	$2(C_6H_{12}NO_2)Pb$

When fused with caustic potash, leucine yields valerate and carbonate of potassium, while ammonia and hydrogen are set free, as follows:—

$$C_6H_{13}NO_2 + 3KHO = KC_5H_9O_2 + K_2CO_3 + NH_3 + 2H_2.$$

Under certain conditions potassium cyanide is also formed, thus—

$$C_6H_{13}NO_2 + 2KHO = KC_5H_9O_2 + KCN + H + 2H_2O.$$

An aqueous solution of leucine is decomposed by nitrous acid, giving leucic acid ($C_6H_{12}O_3$)

$$2(C_6H_{13}NO_2) + N_2O_3 = 2(C_6H_{12}O_3) + 4N + H_2O.$$

This decomposition is exactly comparable to those others by which glycolic and lactic acids are produced from glycocine and alanine when these latter substances are similarly treated.

Heated to 230° in a current of hydrochloric acid gas, leucine loses an atom of water and forms leucimide ($C_6H_{11}NO$).

According to Schwanert, when a watery solution is subjected to a current of chlorine gas it yields leucine hydrochloride, valeronitrile, and dichlorovaleronitrile—

$$7(C_6H_{13}NO_2) + 8Cl = 6(C_6H_{13}NO_2,HCl) + C_5H_7Cl_2N + CO_2.$$

Leucine also yields valeronitrile when distilled with dilute sulphuric acid and peroxide of manganese, thus—

$$C_6H_{13}NO_2 + O_2 = C_5H_9N(\text{Valeronitrile}) + CO_2 + 2H_2O.$$

On the other hand, when distilled with peroxide of lead and water, leucine gives ammonia, butyric aldehyde, and carbonic anhydride.

As already stated, leucine is known to be amido-caproic acid, or $C_6H_{11}(NH_2)O_2$, and this constitution is confirmed both by its modes of decomposition and also by the synthesis effected by Limpricht. This latter consisted in boiling the compound of valeric aldehyde and ammonia with an excess of hydrocyanic and hydrochloric acids until the oily liquid which is at one time produced has disappeared. The following equation illustrates the synthesis:—

$$C_5H_{10}O,NH_3 + HCN + HCl + H_2O = C_6H_{13}NO_2 + NH_4Cl.$$

Purification, Properties, and Decompositions of Tyrosine.

Tyrosine ($C_9H_{11}NO_3$) is obtained as described under leucine, and may be purified by solution in hydrochloric acid and precipitation with sodium acetate, digestion with animal charcoal, if necessary, being previously resorted to with the acid solution. Or the crude crystals may be dissolved in potash and reprecipitated with acetic acid, or recrystallised from ammonia. When very much coloured it is best to convert the tyrosine into hydrochloride.

It forms long fibrous crystals, of a silk-like lustre (when compressed) and white colour, which are very sparingly soluble in cold water, alcohol, and ether. In boiling water, however, tyrosine readily dissolves, as also in acids and alkalies, giving in these cases compounds soluble in alcohol.

It forms a number of unstable metallic compounds, among the principal ones being those represented by the formulæ, $C_9H_9BaNO_3, H_2O$; $2(C_9H_{10}NO_3)Ba$; $C_9H_9Ag_2NO_3, H_2O$; and $2(C_9H_{10}AgNO_3)H_2O$.

The acid combinations, $C_9H_{11}NO_3,HCl$; $C_9H_{11}NO_3, HNO_3$; and $C_9H_{11}NO_3.H_2SO_4$, are all crystalline, but are all partially decomposable by water.

The colligated acid produced by treating tyrosine with fuming sulphuric acid, when neutralised by lime, filtered, and mixed with ferric chloride, gives a peculiar violet solution. Another delicate test of tyrosine is afforded by the red precipitate which is obtained when its solution is heated with a nearly neutral solution of mercuric nitrate. This precipitate is a body of the formula $C_9H_9(NO_2)_2NO_3Hg$.

By cautious distillation, tyrosine yields almost exclusively ethyloxyphenylamine and carbonic anhydride—

$$C_9H_{11}NO_3 = C_6H_5O,C_2H_5NH + CO_2.$$

Oxidised with nitric acid it yields at first, yellow crystals of the nitrate of nitrotyrosine ($C_9H_{10}(NO_2)NO_3$, HNO_3), (having itself further powers of combination with acids and bases), and by further oxidation there is produced nitrotyrosic acid, $C_9H_{10}(NO_2)NO_6$, and subsequently oxalic acid.

By limited oxidation with potassium dichromate and sulphuric acid, tyrosine yields a body of the composition $C_9H_{11}NO_{12},Cr_2O_3,3H_2O$; by further oxidation this is destroyed.

Of the decomposition of tyrosine when fused with potash we have already treated.

CHAPTER XIX.

CHEMISTRY OF ANIMAL CARBOHYDRATES.

The occurrence of a starch-like principle in the liver; the presence of inosite in the brain and muscles; lactose in milk, and grape sugar in the blood and urine in cases of diabetes, makes it worth while to consider a little more in detail what is known about the constitution and relationships of the bodies termed in chemistry 'carbohydrates.' In vegetable chemistry (a subject not intended to be dealt with in this work) their importance is much greater even than in animal chemistry, so that enumeration of the main facts will suffice for the present purpose.

All the carbohydrates apparently contain six atoms of carbon in the molecule, and they also contain hydrogen and oxygen in the proportions in which they co-exist in water. Their assigned formulæ, however, are in many cases but the expressions of empirical composition, and it is left for further researches to establish whether all really contain six atoms of carbon to the molecule, or whether some at least may not contain some multiple of this number of carbon atoms. Many of them are mutually convertible by processes resulting in the abstraction or fixation of the elements of water, while they are also more or less susceptible to processes of fermentation. Again, most of them yield oxalic acid by oxidation with nitric acid, and when treated with a mixture of strong nitric and sulphuric acids, they yield substitution compounds similar to gun cotton; in other words, hydrogen is substituted by peroxide of nitrogen.

From the synthetical researches of Berthelot and others, it would appear that some of the sugars are polyatomic alcohols, like glycerine. Indeed Berthelot has, conjointly with De Luca, prepared a variety of sugar from glycerine. Thus the bodies comprehended in this character may be regarded as hexhydric alcohol of the general formula $C_nH_{2n-4}(OH)_6$. In connection with this part of the subject it is interesting to remember that by the researches of Rosenstiehl and others, it is rendered probable, although not certain, that a kind of sugar may be produced from benzene (C_6H_6) itself. When benzene is treated with hypochlorous acid, direct combination occurs, and the body $C_6H_9Cl_3O_3$ is formed, and when this is treated with sodic carbonate, the following reaction, perhaps, takes place:—

$$C_6H_9Cl_3O_3 + 3H_2O = C_6H_{12}O_6 + 3HCl.$$

Phenose, as this body is termed, is not fermentible, but if its production, in the way described, be hereafterwards confirmed, it is of the greater importance, since it directly connects the so-called carbohydrates with the benzene series and with the fatty acid series.

It should be remarked that closely related to the carbohydrates are a few other bodies which contain hydrogen and oxygen in different proportion, and indeed it is to these substances more particularly that the characters of hexhydric alcohols are ascribed. But this hard and fast line cannot be maintained with any show of reason, although it is to be admitted that the amylaceous and saccharine principles proper, deport themselves not merely as alcohols but also as aldehydes.

In the series of hexhydric alcohols, mannite ($C_6H_8(OH)_6$), from manna (the dried sap of *Fraxinus ornus*), and dulcite ($C_6H_8(OH)_6$), which is isomeric with mannite and obtained from various species of *Melampyrum*, are placed.

The carbohydrates may be conveniently divided into three groups, viz., the glucoses, saccharoses, and starches, and the following table[1] exhibits their formulæ and best known members.

Glucoses	Dextrose (grape sugar)	$C_6H_{12}O_6$
	Lævulose	
	α and β galactose	
	Arabinose	
	Sorbin, Eucalyn	
	Inosite	
Saccharoses	Saccharose (cane sugar)	$C_{12}H_{22}O_{11}$
	Maltose	
	Lactose (milk sugar)	
	Arabin (gum arabic)	
	Melitose, Melizitose, Trehalose	
Starches	Starch, Inulin	$C_6H_{10}O_5$.
	Dextrin, Glycogen	
	Cellulose	

Those members of these different groups which approach sugar or gum in general properties, are soluble in water, while others, like ordinary starch, dissolve in an imperfect sort of way, partaking rather of the nature of diffusion than solution. Cellulose is quite insoluble in water. Again, the saccharoses are convertible into dextrose, lævulose, or galactose, by prolonged boiling with dilute sulphuric acid. Illustrative of these changes the following equation is exemplary:[1]—

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[1] Armstrong, *Organic Chemistry*, p. 186.

$$\begin{array}{ccccccc} \text{Cane Sugar} & + & \text{Water} & = & \text{Dextrose} & + & \text{Lævulose} \\ C_{12}H_{22}O_{11} & + & 2H_2O & = & C_6H_{12}O_6,H_2O & + & C_6H_{12}O_6. \end{array}$$

Further, certain of the compounds hereinbefore mentioned are resolved into anhydride-like principles when carefully heated, and these in their turn are again changed into the original substances by boiling with dilute acids.

Thus dextrose, lævulose, and mannite split up as follows:—

$$\begin{array}{lcl} \text{Dextrose.} & & \text{Glucosane.} \\ C_6H_{12}O_6H_2O & = & C_6H_{10}O_5 + 2H_2O. \\ \text{Lævulose.} & & \text{Lævulosane.} \\ C_6H_{12}O_6 & = & C_6H_{10}O_5 = H_2O. \\ \text{Mannite.} & & \text{Mannitane.} \\ C_6H_{14}O_6 & = & C_6H_{12}O_5 + H_2O. \end{array}$$

Among the glucoses; sorbin, eucalyn, and inosite are distinguished from the other members by the fact that they do not undergo fermentation in the presence of yeast.

Among the saccharoses, cane sugar is first resolved into dextrose and lævulose before it ferments; the same with maltose. Milk sugar is also, probably, first converted into galactose before it ferments.

In the annexed table[2] is summarised the principal properties of a few of the more important glucoses and saccharoses.

Glycogen, which has been more particularly described in the Chapter on Glycosuria, is a substance belonging to the group of starches. It yields dextrose by boiling with

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[1] Miller's *Organic Chemistry*, vol. iii. p. 91 (3rd edition).

[2] *Ibid.* p. 113.

Variety and Origin.	Principal Properties.
GLUCOSES: Dextrose, or grape sugar, $C_6H_{12}O_6.H_2O$; from dried fruits, or from starch by means of acid, or from glycogen of liver, or as found in urine in diabetes.	Crystallises in cubes or square tables. Soluble in water, and more soluble in alcohol than cane sugar. Is precipitated by ammoniacal lead acetate, reduces potassio-cupric tartrate mercury, silver and gold, from their boiling solutions. Ferments readily with yeast; produces right-handed rotation = 57·4°; yields saccharic and oxalic acids with nitric acid.
Lævulose: From recent fruits, and from cane sugar by action of acids, &c., $C_6H_{12}O_6$.	Is not crystallisable; is soluble in dilute alcohol; is not precipitated by subacetate of lead; reduces alkaline potassio-cupric tartrate; yields a left-handed rotation, = − 26° (at 15° C.); undergoes alcoholic fermentation with yeast, and is partially convertible into grape sugar by long boiling with dilute acids.
Inosite: From brain matter and muscular tissue, $C_6H_{12}O_6,2H_2O$.	Crystallises in radiated tufts; soluble in water; insoluble in alcohol and ether; loses its water of crystallisation at 100° C., fuses at 210° C., and loses more water; is without action on polarised light; does not reduce Fehling's solution; is not susceptible of alcoholic fermentation, but undergoes fermentation with cheese and chalk, yielding lactic and butyric acids. Is not changed by boiling with dilute acids; is precipitated by ammoniacal lead acetate.
SACCHAROSES: Cane sugar. Or sucrose, from sugar-cane, $C_{12}H_{22}O_{11}$.	Crystallises in rhomboidal prisms; very soluble in water, and less so in dilute alcohol. Fuses at 160° C.; is not precipitated by subacetate of lead, but only by ammoniacal lead acetate. Does not reduce Fehling's solution; produces a right-handed rotation = 73·8°; undergoes alcoholic fermentation with yeast. Splits up by boiling with dilute acids into dextrose and lævulose.
Lactose: Or milk sugar, from whey of milk, $C_{12}H_{22}O_{11},H_2O$.	Crystallises in four-sided prisms; is not so soluble in water as grape sugar; nearly insoluble in alcohol and ether; is precipitated by ammoniacal lead acetate; reduces alkaline solutions of copper, silver, and mercury when boiled with them; produces right-handed rotation = 56·4°; is converted into galactose by boiling with dilute acids, and yields mucic and oxalic acids on oxidation with nitric acid.

dilute acids, or by contact with diastase, saliva, pancreatic fluid, and other soluble ferments.

Very little is known about the constitution of the starches, but some researches which O'Sullivan has recently contributed to the 'Journal of the Chemical Society' are likely to lead to some important decisions as regards the changes and relationships of certain members of this group and the approximating groups of glucoses and saccharoses.

CHAPTER XX.

ON THE FATS AND FATTY ACIDS OF THE HUMAN BODY.

THE term 'fat' is applied to a great number of similarly constituted principles of wide occurrence in the animal and vegetable worlds, and the precise history of the function of fat in the system is one of the most interesting subjects in animal chemistry.

It is entirely unnecessary to give more than a general description of the nature and properties of fats, for their chemical bearings are not sufficiently known to enable us thoroughly to understand how they are produced, or the exact steps by which they are resolved into other substances in the body.

Chemically, they may all be viewed as derivatives of the triatomic alcohol glycerine ($C_3H_5(HO)_3$), in which the hydroxylic groups are replaced by the radicles of fatty acids. So far as most of the fats are concerned, the fatty acids yielded on decomposition belong to the series $C_nH_{2n}O_2$; thus palmitin, margarin, and stearin give acids belonging to this series. Other fats, such as olein, give acids of the series $C_nH_{2n-2}O_2$. There seems to be, however, a definite relation between the acids of these two series—a consideration more particularly pointed out in the Chapter on the Pettenkofer Reaction.

Stearic acid ($C_{18}H_{36}O_2$), when pure, is a white crystalline substance, melting at 70·5° C.; while palmitic acid ($C_{16}H_{32}O_2$), which is also white and crystalline, melts at 62° C. Stearic acid may be obtained in beautiful colourless, transparent, rhombic plates by recrystallisation from alcohol, while by a similar process palmitic acid may be obtained in tufts of delicate needles.

Margaric acid ($C_{17}H_{34}O_2$) is, according to Heintz, a mixture of palmitic and stearic acids, nevertheless it is by no means certain that an individual acid of this formula does not exist; and indeed it has been shown (where treating of Brain Chemistry) that its existence is highly probable.

Oleic acid ($C_{18}H_{34}O_2$) is fluid at ordinary temperatures, and when fused gently with caustic alkalies, yields palmitic acid and acetic acid, thus:—

$$C_{18}H_{34}O_2 + 2KHO = C_{16}H_{31}KO_2 + C_2H_3KO_2 + 2H.$$

All these fatty acids are readily soluble in warm alcohol, and much more so in ether, benzene, &c. When present in admixture, they may be separated by various methods.

(1) By fractional crystallisation from alcohol; the earlier crops containing more stearic acid, and the ultimate mother liquors most of the oleic acid.

(2) By dissolving in hot dilute ammonia water, reprecipitating the acids by neutralisation, cooling, and pressure of the product between folds of porous paper. In this way most of the oleic acid may be separated.

(3) By converting into barium salts, and extracting the dried salts with boiling absolute alcohol. Only oleate of barium dissolves (to the extent of 5 grms. per litre).

(4) By making into lead salts, and extraction of the

lead compounds with ether. Oleate of lead dissolves, and this by decomposition with hydrochloric acid, yields the free acid which may be extracted by ether.

(5) The mixture of palmitic and stearic acids, freed from oleic acid, may be differentiated by fractional crystallisation from alcohol, or the alcoholic solution may be fractionally precipitated by means of an alcoholic solution of lead, barium, or magnesium acetate. The most insoluble parts of the precipitates (viz. those obtained earliest) contain most stearic acid, while the later ones contain more palmitic acid, and by a repetition of these processes upon the various fractions—or better, the extreme products—a tolerable separation may be effected.

I refrain from entering into any further study of the fatty acids or their derivatives, because what is known is not sufficient to reveal their general relations with other groups of bodies, and until these are ascertained it is impossible to make those physiological considerations which should properly follow upon them.

From the gradation of character exhibited by various fats, and inasmuch as in nature they occur for the most part in admixture, it is extremely difficult to isolate them in an absolutely pure state, and thus it arises that in all probability there exists in nature a much larger number of fats than are at present established as known.

For instance, up to quite recently, melissic acid ($C_{30}H_{60}O_2$) was the highest known member of the series of acids indicated by the general formula $C_nH_{2n}O_2$, but I have since shown[1] that there can be obtained from cocoa butter a crystalline acid (Theobromic acid) presenting an empirical formula certainly as high as $C_{64}H_{128}O_2$, and perhaps higher, while this is accompanied by another new solid and crystalline acid probably lower than lauric acid ($C_{12}H_{24}O_2$) in the series.

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[1] *Journ. Chem. Soc.*, January 1878.

In the same paper certain considerations are stated which render it probable that there may exist fats having a more complex structure than the better known members. For instance, while ordinary fats have the three hydroxyls of glycerine substituted by three molecules of the same fatty acid radicle, there probably exist fats in which the three hydroxyls are substituted by three different fatty acid radicles. Thus taking the formula of ordinary palmitin to be

$$C_3H_5 \left\{ \begin{array}{l} C_{16}H_{31}O_2 \\ C_{16}H_{31}O_2 \\ C_{16}H_{31}O_2, \end{array} \right.$$

it is conceivable that cocoa butter has a formula not far removed from

$$C_3H_5 \left\{ \begin{array}{l} C_{12}H_{23}O_2 \\ C_{64}H_{127}O_2 \\ C_{18}H_{33}O_2. \end{array} \right.$$

All fats when treated with water in sealed tubes, or submitted to superheated steam, or boiled with alkalies, split up, yielding glycerine and fatty acids. Thus tristearine, when saponified with caustic soda, is decomposed, as expressed by the following equation :—

$$C_3H_5(C_{18}H_{35}O_2)_3 + 3NaHO = C_3H_5(HO)_3 + 3C_{18}H_{35}NaO_2 ;$$

that is to say, glycerine is set free and stearate of sodium is formed.

Although butyric acid ($C_4H_8O_2$) is found in the sweat, and fatty acids are found in an emulsed state in the body, yet it can scarcely be said that fatty acids enter into the composition of the body itself. Where they occur, they are intermediate products of change, which are either elaborated in the body into fats, or oxidised in the blood, or given off as excretive products. In fact, from a number of considerations, it almost necessarily follows that the fat which is formed in the body and exists there in adipose tissue or otherwise, is constructed within the body.

Fat cells (*folliculi sebacei*) are scattered over the whole surface of the body, and secrete a peculiar fat which keeps the skin supple and flexible. It does not appear to have a constant composition, and it is associated with other principles, as shown by the following analysis of Esenbeck,[1] conducted upon the fat secreted by an enlarged sebaceous gland :—

Stearin	24·2
Extractive matter, with some olein	12·6
Salivary matter	11·6
Albumin with casein (?)	24·2
Phosphate of calcium	20·0
Carbonate „ „	2·1
Carbonate of magnesium	1·6
Traces of acetate and chloride of sodium, and loss	3·7

Aggregations of fat cells also may and generally do occur in many parts of the body, as in the orbit, about the heart and kidneys, &c. When present in other parts, their presence chiefly depends upon the state of nutrition and individual habits, and ordinarily such accumulations are regarded as a reserve stock formed from excessive nutriment.

These accumulated globules form masses which are either suspended in fluids or lodged between fibres.

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[1] Taken from Simon's *Animal Chemistry*. Sydenham Society edition.

Of the relation of fat in the body to the function of respiration and nutrition, cognisance has been taken in other chapters.

If in any part of the body oxidation is impeded, there fat forms, as for instance is the case in fatty degeneration of the heart and liver (?).

Human fat melts at about 63° C., and contains palmitin, $C_3H_5(C_{16}H_{31}O_2)_3$; stearin, $C_3H_5(C_{18}H_{35}O_2)_3$; and olein, $C_3H_5(C_{18}H_{33}O_2)_3$, together, perhaps, with others whose constitutions have not been established. That this is so, is the more probable considering the close relation existing between fats, saccharides, and the phosphorised principles of brain matter. These latter, indeed, may be regarded as synthetical products formed from fats and other matters capable of presenting phosphoryl and nitrogenous bases in a suitable form for combination. (See Chapter on Brain Chemistry.)

Before proceeding to discuss the formation of fat in the body, it may be worth while to point out a little more closely the intimate chemical relation between starch, sugar, and saccharides, and glycerine and glycerides; and between glycerides and the phosphorised principles of nervous tissue. Ordinary starch has the formula $C_6H_{10}O_5$, and may be resolved into glucose by the assimilation of water. The glucose thus formed seems to be a kind of alcohol, just as glycerine is, and as glycerine is capable of forming fats, or glycerides, by reaction with fatty acids, so glucose and other forms of saccharine principles similarly give rise to glucosides, saccharides, &c. Thus we have

(1) $C_6H_{10}O_5 + H_2O = C_6H_{12}O_6$
(2) $C_3H_8O_3 + 3C_{18}H_{36}O_2 - 3H_2O = C_3H_5(C_{18}H_{35}O_2)_3$
(3) $C_6H_{12}O_6 + 2C_{18}H_{36}O_2 - 3H_2O = C_{42}H_{78}O_7$.

The saccharide formed as in the last given equation is illustrative of a great number of similar bodies which in their chemical properties are closely related to the fats, and like the latter are resolved by saponification processes into the principles from which they were originally formed.

Then again, glycerides are seen to be related to the phosphorised brain principles by the following general formulæ :—

Fats. Phosphorised Brain Principles.

$$C_2H_5\begin{cases}\text{HO, substituted by fatty acid radicle}\\ \text{HO,} \quad " \quad " \; " \quad " \quad "\\ \text{HO,} \quad " \quad " \; " \quad " \quad "\end{cases} \qquad C_3H_5\begin{cases}\text{HO, substituted, \&c.}\\ \text{HO,} \quad " \quad "\\ HO(OPO)C_5H_{13}NO_2.\end{cases}$$

These matters, here pointed out so briefly, are replete with scientific interest, and are sufficient to furnish material for research at the hands of chemists and animal chemists for many years to come.

Thus to the chemist it would be of peculiar importance to construct corresponding phosphorised and nitrogenous principles (to those above symbolised) from saccharine principles, while for the physiological chemist these connecting links between series of bodies throw a light upon the exact *modus operandi* employed by nature in her marvellous work of synthesis.

This chapter may be fitly concluded with some observations taken from an excellent historical summary[1] of the various views which have been held regarding the formation of fat in the body. These different views have been propounded since the discovery that the fat taken by animals in their food is insufficient to account for all the fat stored in the body. Liebig originated the doctrine that carbohydrates contained in the food is the source of such fat, and this view has been supported by Gundlach, Huber, Dumas, Milne-Edwards, Boussingault, Lehmann, Grouwen, Lawes and Gilbert, and Pasteur. But C. Voit contended that the fat other than that ready formed in the food, was derived from the nitrogenous parts of the food, and not from the carbohydrates (such as starch). Stohmann, G. Kuhn, Pettenkofer, and others, by their experiments lent support to this view. The formation of adipocere demonstrated the possibility of a conversion of nitrogenous tissue into fat, as indeed seems to take place in the case of fatty degeneration of whole organs. Moreover, other observers showed that fat could be formed at the expense of casein, and a number of physiological experiments seemed to indicate the same or similar truths. Again, F. Hofmann claimed to have proved that the fat ready formed in food can pass into the animal cells without change and be stored, while Toldt and Subotin denied this proposition. It must be confessed as more probable that the absorption and deposition of the fat is preceded by its saponification during digestive processes, much in the same way as albuminous substances are first reduced to the state of peptones and then reconstructed as tissue afterwards.

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[1] By H. Weiske and E. Wildt (*Zeitschr. f. Biologie*, x. 1–20).

Weiske and Wildt express an opinion which merits great consideration from the fact that it is borne out by a most careful research. Animals were subjected to a monthly weighing when fasting; the daily food administered was weighed and analysed; the fæces were also weighed and analysed, while the bodies of the animals operated upon were slaughtered and also submitted to analysis. As a result then of this research, the opinion was formed that while there is no direct proof of the conversion of proteids into fat when food rich in nitrogen is administered to *omnivora*, there is evidence in this case, as also when food poor in nitrogen is given, that the digested proteids suffice to cover not merely the increase of flesh, but also the whole of the fat laid up in the body.

From what is known regarding the decomposition products of albuminous principles,[1] it is not improbable that Voit's theory is correct in some measure, but it by no means follows that Liebig's theory is not partly true. Further investigations must decide these matters.

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[1] See Schützenberger's researches, described in Chapter xviii., on Albuminous Substances.

CHAPTER XXI.

THE PETTENKOFER REACTION.

It was observed many years ago by Pettenkofer,[1] that when cholic acid ($C_{24}H_{40}O_5$) was treated with strong sulphuric acid in the presence of cane sugar, a beautiful violet colour ensued, and he founded upon this reaction a test for bile and for sugar. Since the time in question it has been ascertained that choloidic acid ($C_{48}H_{78}O_9$), and dyslysin ($C_{48}H_{72}O_6$), which are derived from cholic acid by the abstraction of water, also give the reaction, as well as the conjugated compounds—glycocholic and taurocholic acids—which yield cholic acid by a simple process of decomposition. Hyocholic acid ($C_{27}H_{43}NO_5$), and hyocholalic acid ($C_{25}H_{40}O_4$), as well as those dehydrated derivatives which may be obtained from the latter substance, also furnish with sulphuric acid and sugar the Pettenkofer reaction.

In treating of Bile and its chemistry, various reasons have been assigned for the belief therein expressed, that these compounds above named are more or less directly related to oleic acid ($C_{18}H_{34}O_2$), which it has been observed also furnishes the colour test under description. That the connection of biliary acids with the fatty acids of the series $C_nH_{2n}O_2$, although not yet known, is still (probably) of a very definite character is sustained by the later observations of Kingzett and Hake,[1] of which more anon.

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[1] *Ann. Chem. Pharm.* lii. p. 90 (1844).

Gradually a number of substances supposed to have no relation to the biliary acids have been discovered to yield the Pettenkofer reaction with sulphuric acid and sugar, while yet again a number of other bodies give the reaction with sulphuric acid alone. Pettenkofer himself, although he attempted to isolate the coloured principle, was not successful, nor could he offer any explanation of the reaction. Since then, until quite recently, its further study has not been effected, if we except some few attempts on the part of several observers to diagnose between the colours given by various substances by means of an examination of the absorption spectra. Kingzett and Hake have, in their paper already referred to, continued the study of the reaction, and, beyond making a large number of new observations, have offered an explanation of it. Before giving this, it will be best to arrange the substances which yield the reaction in two tables, viz., one including those which give the reaction with sugar, and those which give it with sulphuric acid alone (without sugar).

Substances which give the Pettenkofer Reaction with Sulphuric Acid and Sugar.

Cholic acid	$C_{24}H_{40}O_5$
Choloidic acid	$C_{48}H_{78}O_9$
Dyslysin	$C_{48}H_{72}O_6$
Taurocholic acid	$C_{26}H_{45}NSO_7$
Glycocholic "	$C_{26}H_{43}NO_6$
Hyocholic "	$C_{27}H_{43}NO_5$
Hyocholalic "	$C_{25}H_{40}O_4$
Lithofellic "	$C_{20}H_{36}O_4$
Oleic "	$C_{18}H_{34}O_2$

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[1] Paper read before the London Chemical Society, January 18, 1877, and printed in *Pharm. Journ.* May 12, 1877.

Substances which give the Pettenkofer Reaction with Sulphuric Acid and Sugar—continued.

Thudichum	Cholesterine	$C_{26}H_{44}O$
	Lecithine	$C_{43}H_{84}NPO_8$
	Myelines, one of which is	$C_{84}H_{165}N_3P_2O_{13}$
	Kephaline	$C_{42}H_{79}NPO_{13}$
Kingzett and Hake	Benzene	C_6H_6
	Phenol	C_6H_6O
	Turpentine, clove, and other oils	$C_{10}H_{16}$; $C_{15}H_{24}$
	Camphor	$C_{10}H_{16}O$
	Salicylic acid	$C_7H_6O_3$
	Pyrogallic acid	C_7H_6O
	Tannic acid	$C_{27}H_{22}O_{17}$
	Morphine	$C_{17}H_{19}NO_3,H_2O$
	Rape, cotton seed, colza, and other mineral oils containing	$C_{18}H_{34}O_2$
	Various fats.	

Substances which give the Pettenkofer Reaction with Sulphuric Acid alone.

	Cod-liver oil (this contains oleic acid, a phosphorised fat, and acetin).	
Thudichum	Cerebrine	$C_{34}H_{66}N_2O_8$
	Stearoconote	$C_{34}H_{66}N_2O_8$
	Phrenosine	$C_{34}H_{67}NO_8$
	Kerasine	$C_{46}H_{91}NO_9$
Posselt	Hederic acid (from ivy)	
Kingzett and Hake	Piperine	$C_{17}H_{19}NO_3$
	Salicin	$C_{13}H_{18}O_7$
	Phloridizin	$C_{21}H_{24}O_{10}$
	Coniferin	$C_{16}H_{22}O_8,2H_2O$
Kingzett	Scammony resin.	

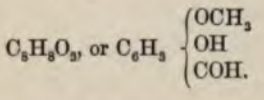
Now if we take those substances embraced in the second table, it is seen that they give the Pettenkofer reaction with sulphuric acid alone, because they all contain a sugar nucleus or yield glucose by proper treatment, thus rendering the addition of sugar unnecessary. Thudichum has shown (as already explained when treating of the chemical constitution of the brain) that cerebrine, its isomer stearoconote, and the allied bodies phrenosine and kerasine, give glucose when they are boiled with dilute sulphuric acid or with baryta water, both of which reagents act through the fixation of water: indeed the decomposition may be effected by water in sealed tubes. I have shown [1] that hederic acid and resin of scammony give glucose by a similar treatment. Salicin is known also to do the same, splitting up into saligenin or salicylic alcohol and glucose by acids, thus:

$$C_6H_4(OH)CH_2(OC_6H_{11}O_5) + H_2O = C_6H_{12}O_6 + C_6H_4(OH)CH_2OH$$

while the decomposition of phloridizin takes place as represented by the equation—

$$C_{21}H_{24}O_{10} + H_2O = C_6H_{12}O_6 + C_{15}H_{14}O_5.$$

Again, Tiemann and Haarman have shown that coniferin crystals decompose into glucose and a crystalline substance $C_{10}H_{12}O_3$ which yields on oxidation a methyl ether of protocatechuic aldehyde—



$$C_8H_8O_3, \text{ or } C_6H_3 \begin{cases} OCH_3 \\ OH \\ COH. \end{cases}$$

Thus the whole list is accounted for excepting piperine and cod-liver oil, and these will probably present no difficulty when we know more about their constitution. As it is, the case of cod-liver oil admits, to some extent, of an explanation. It is known to contain acetin, a phosphorised principle like myelin, and oleic acid. Now the latter two would give with strong sulphuric acid, if sugar were also present, the Pettenkofer reaction, and it is a significant fact that acetin is a compound derived from acetic acid and glycerine; significant because it is known that in certain instances acetic acid may take the place of sugar.

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[1] *Pharm. Journ.* September 15 and 22, 1877.

From what is known, therefore, Kingzett and Hake conjectured that the coloured substance which is produced in the Pettenkofer test is a body derived from a benzene derivative (of a certain type) and glucose, by the abstraction of the elements of water on the one hand, and their unison on the other hand through the same synthetical influence of the strong sulphuric acid; indeed the authors are inclined to believe that sulphuryl forms an integral part of the compound molecule. The fact that piperine gives the reaction with sulphuric acid alone, while its isomeric morphine only gives it in the further presence of sugar, is one which in its investigation will probably explain the isomerism of these substances; it is not improbable that piperine will prove to be a glucoside. The researches of Fittig and Mielck on piperic acid are not opposed to this notion. To make a generalisation then, it may be said that, so far as observed, all those substances which give the Pettenkofer reaction with sulphuric acid alone, without, that is to say, the addition of sugar, yield sugar by a simple process of hydration, and therefore contain a radicle related to sugar in their own constitution. In such cases the strong sulphuric acid splits up the compound, and the constitutional groups are re-arranged by it in such a way as to produce the coloured compound.

In those other cases where it is necessary to add sugar before sulphuric acid produces the reaction, there must be present some group which under the influence of the acid is brought into combination with the sugar, the product being also a coloured compound. With the object of ascertaining the particular nature of the group in question, Kingzett and Hake have made many experiments which are yet in progress by one of them. The following is among the most interesting of their results.

Special Investigation of certain New Reactions and Theoretical Considerations with regard to their Meaning.—When camphor ($C_{10}H_{16}O$) is placed in strong sulphuric acid it readily dissolves, forming a yellowish red solution: when saturated the solution is of a deep red colour, and it is only upon long standing that a slight odour of sulphurous anhydride is apparent, otherwise the solution has a weakened camphor odour. This product gives with cane sugar a most beautiful reaction; the colour is, however, as in all cases, quickly destroyed by water. From the solution of camphor in sulphuric acid, water precipitates a substance free from sulphur, and having, so far as observed, all the properties of the original camphor. Nevertheless, from what is to be described hereafter, it appears that in the sulphuric acid solution it exists as a sulpho-acid. When such a solution is treated with sugar, and water added to the product, there results a precipitate which is slightly yellow, and after washing exhibits a tendency to cake. It is free from sulphur, but is competent to furnish, with strong sulphuric acid alone, the original violet colour in an intense degree. This result seemed at first sight to indicate that the body produced as described, was a saccharide or a glucoside, and to gain information on this point many experiments were conducted, as follows:—A saturated solution of camphor in sulphuric acid was exposed to a freezing mixture, and treated with its own volume of concentrated cane sugar solution, stirring meanwhile. By adding the sugar drop by drop, the temperature was kept throughout below

15° C., and carbonisation of the sugar was thus prevented. There formed a solid pasty pink mass, which was then treated with much water; frothing ensued, and gradual destruction of the colour. The mixture was then filtered and the precipitate well washed. On boiling it with a very dilute solution of sulphuric acid during three hours, the purple colour to which allusion has been made, formed upon the warm sides of the dish, but ultimately no sugar could be detected in the solution by means of the copper test. From this it follows that the substance cannot be a saccharide, in the ordinary sense of that term. Nevertheless it is probable that strong sulphuric acid has the power, possibly by the abstraction of water, of entering into combination conjointly with the camphor and sugar residues. Such a constitution seems at the first blush to express the nature of the coloured body. When treated with water, sulphuric acid is re-formed, and there results a combination which only requires strong sulphuric acid again to restore primary conditions.

The relations existing between cholic acid, choloidic acid, dyslysin, taurocholic, glycocholic, hyocholic, hyocholalic, and lithofellic acids are fairly well known. They all appear to contain a similar residue, and where the difference is not one of the elements of water, or conjugation, it is one of homologity. From what we know too of cholic acid, it appears to be connected in some way with oleic acid, while lecithine yields oleic acid on hydration. The myelines and kephaline give by hydration, among other decomposition products, acids which appear to possess an intimate relation to the biliary acids. That cholesterine contains a group identical with one present in cholic acid, is known because they both yield cholesteric acid by oxidation with nitric acid. The direct relations between the foregoing bodies and those benzene derivatives which Kingzett and Hake have found to yield the Pettenkofer test with sulphuric acid and sugar are altogether unknown, but will probably be revealed by further studies of the fatty acids of the series $C_nH_{2n}O_2$.

Pettenkofer himself showed that strong hydrochloric acid could be used in his test in place of the sulphuric acid, but stated that the intensity of the colour was not so striking. Since then it has been shown that acetic acid may sometimes take the place of the sugar.[1] Pettenkofer also observed that any body which by contact with strong acid is resolved into glucose, could replace the sugar. Mannite, which is not so transformed, cannot take its place. Kingzett and Hake have shown that inulin ($C_6H_{10}O_5$) and potato starch may each be used in the place of cane sugar, if at the same time a trace of water be present. More water destroys the colour under all conditions. At present, therefore, the only safe conclusion which may be inferred from all these considerations, is that the coloured body produced by the action of strong sulphuric acid upon various bodies and sugar, depends for its colour more upon the constitution than the composition of the product.

This subject has been dealt with in detail because it brings the chemistry of the bile and the brain into intimate connection, and it is by a further study of these and blood chemistry that this connection will be established and confirmed.

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[1] The empirical formula of acetic acid, when multiplied by 3, gives that of glucose.

CHAPTER XXII.

ON FERMENTATION, PUTREFACTION, AND THE GERM THEORY OF DISEASE: ALSO ANTISEPTICS AND DISINFECTANTS.

THE ground which is covered by the subject matter of this chapter is so large that it is utterly impossible to consider any one phase at all in detail. It will, therefore, be best to summarise all phases of the subject, and to indicate the position assumed to-day by the different schools of thought.

In doing this, I shall endeavour to regard the subject entirely from a chemical point of view, with the object of indicating how deeply concerned chemistry is with all processes of infection and disease.

When a solution of sugar is exposed to the action of healthy yeast it suffers a change; the atoms comprised in its molecule are broken up and rearranged into new forms, which are recognised as alcohol and carbonic dioxide. Glycerine and succinic acid are also formed at the expense of the sugar, but the lactic acid which generally accompanies alcoholic fermentation is considered as proved to be due to the presence of a ferment distinct from, but accompanying, the yeast. The explanation which this phenomenon has received at the hands of Pasteur—an explanation now all but universally accepted—is as follows. The fermentation alluded to, is regarded as a particular instance of a biological reaction manifesting itself as the result of a special force residing in organisms; or, in other words, fermentation is essentially 'a correlative phenomenon of a vital act, beginning and ending with it.'

On this hypothesis, whenever there is fermentation there is organisation, development, and multiplication of the globules of the ferment itself. The instance quoted above is by no means solitary; it is exemplary of many other changes, induced by the same or other ferment matters in media suitable for their growth and reproduction. Thus, we have the mannitic, lactic, ammoniacal, and butyric fermentations, besides many others, all of them having one feature in common, viz., the reproduction of the ferment.

Some of these processes have been studied with all the power of scientific imagination and reasoning, supplemented by the most refined methods of research available. Pasteur has described the life processes of yeast cells, and their multiplication by budding or by throwing off spores. Even their composition has been elucidated to some extent, although not to the principal extent. The ash of yeast cells consists essentially of phosphoric acid and potassium, together with a little magnesium and a trace of calcium, and this knowledge enables the operator to construct a medium in which yeast will flourish and reproduce itself. But of the character of the organic nitrogenous constituents of yeast next to nothing is known. It is certainly known that almost any albuminous substance dissolved in the medium will suffice as food to the yeast plant, but of the albuminous parts of the plant itself we have no precise information. The various conditions upon which the health, and even disease of yeast and other cells depend, have been beautifully elucidated by Pasteur, and it is thought that the yeast plant respires like the higher forms of animal life, and that when free oxygen is not available it is capable of obtaining it from sugar if present. An experiment devised by Schützenberger (and one to which previous reference has been made) for demonstrating the respiratory function of yeast deserves mention here. He caused arterial blood to circulate slowly through a system of hollow tubes, constructed of thin gold-beater's skin, and immersed in a mixture of yeast diffused in fresh serum kept at 35° C. As the blood passed out at the other extremity, it was seen to be black and venous, owing to the abstraction of oxygen from it by the yeast.

One of the main questions to be solved in such inquiries as those of Pasteur, is whether different acts of fermentation are due to different and individual ferments, and to illustrate some of the results which have been obtained in this direction, reference may be made to some recent experiments of Professor Lister upon the lactic fermentation, or that change in milk which is accompanied by its coagulation and the production of lactic acid from the sugar originally contained in it. Of course by the observance of proper precautions, milk may be kept in an unchanged condition, quite free from acidity and curdling; but of this more anon. When, however, it is not subjected to these precautions, microscopic observation always reveals the presence of minute organisms—bacteria—in the coagulated milk. According to the recent experiments of Lister, these bacteria are not uniform in character, but comprise two or more varieties, to one of which is due the special change adverted to. This was shown as follows. It was endeavoured to estimate the number of bacteria in a given quantity of sour milk, by counting the number visible in a small measured drop placed upon a microscopic glass slide; then the milk was diluted so that a single drop would probably contain on the average one bacterium. With such measured quantities, further amounts of fresh boiled milk were inoculated, and out of five glasses so treated only one curdled, and on examination proved to contain *Bacterium lactis*. Having thus succeeded in cultivating the particular bacterium in question, it was easy to inoculate any further quantities of milk. The chief points established by these results are, first, that the ferment causing the curdling was not in solution in a dissolved state, or else all the samples of milk inoculated would have curdled, but present in particles; and second, that to the one particular bacterium—*Bacterium lactis*—as Lister terms it, is due the lactic fermentation.

Liebig, who thought deeply and wrote well upon the questions under study, held somewhat different views regarding fermentation, and even the last paper written by this illustrious chemist consisted of a refutation of the later inferences of Pasteur. Of course, as regards the ultimate results of fermentation, all are agreed; but men differ in their views of the acting causes. Thus, Liebig neglected, to a certain extent, the element of life, and regarded fermentation as due to a disturbance of the equilibrium imparted to the elements of bodies by virtue of an existing change or motion in other bodies in contact with them. But, after all, when broadly considered, the difference presented by the views held by Liebig and those of Pasteur as generally understood, is not so great as appears at first blush. In support of our meaning, let us take the form of fermentation which is supposed by Bernard to cause the transformation of the glycogen of the liver into glucose. The change here effected is one of hydration, and, upon the germ theory, this change is supposed to be due to the influence of a special ferment present in the liver or the blood, which, while it thus acts, reproduces itself from a part of the matter influenced in the reaction. Well, Liebig would rather have viewed the change as apart from vitality; it was enough for him to perceive the conditions existing necessary to the transformation of starch into sugar, by the assimilation of the element of water; he did not see the reason for believing the change to be necessarily due to a form of life; all that was required was the presence—the contact—of a body itself in course of a certain kind of change.

Previously, Berzelius had entertained some such notion of catalysis or contact action, but he supposed that the agent which induces the change remains itself unchanged. Such an idea as this latter one is untenable in the present state of knowledge regarding matter and force. It may be asserted as an axiom that no substance can bring about any result among other substances without itself suffering change in some respect, be it physical or chemical. Thus, for instance, the yeast which causes alcoholic fermentation, while it is reproduced it is yet destroyed, and although the yeast assumes no constitutional part in the products of the changed sugar, some of it breaks down and dies, and undergoes a specific set of reactions, none the less real because unexplained.

Liebig, then, maintained that a body in state of change may communicate to some other bodies with which it may come in contact, a state of change also, without being apparently altered. In fact, Liebig's views, which often receive a good deal of misrepresentation, may be expressed thus: Mechanical or any other motion exerts an influence on the power which determines the state of a body. Thus, a crystal of sulphate of sodium, a speck of dust, or grain of sand, when dropped into a saturated solution, say of sulphate of sodium, may determine the entire crystallisation of the fluid. Or again, when the fulminates of silver and mercury are tickled lightly by a feather or glass rod, they suddenly explode with violence. A still better instance, and one to which Liebig seemed particularly attached, is the reaction which occurs between peroxide of hydrogen and argentic oxide; these substances, when mixed, give rise to the production of metallic silver and free oxygen, thus—

$$H_2O_2 + Ag_2O = H_2O + Ag_2 + O_2.$$

The peroxide of hydrogen, being unstable, is constantly undergoing decomposition from the moment of its formation, and this decomposition results in the production of water and free oxygen; immediately, therefore, that this substance comes into contact with oxide of silver, it gives to that body the same tendency to change.

Brodie explains the result differently. He says the second oxygen atom in the peroxide of hydrogen is in a different polar condition to that of the oxygen in the silver compound, and, therefore, one being negative and the other positive, they, having an attraction, combine. But this is no advance on the fact; it is merely a word explanation—another way of expressing the same fact, and it is not exempt from criticism, because it does not take into consideration the liability of peroxide of hydrogen itself to decompose.

Without multiplying examples illustrative of Liebig's views, we may say there is nothing inconsistent in their principal features and those of the doctrines now more widely held to-day. In fact, Pasteur and others have but advanced on Liebig's hypothesis. Pasteur's doctrines confine themselves to fermentative phenomena in which low forms of life are undoubtedly the active agencies, and these observations have led inevitably to speculations on germs, their nature, propagation, and functions, and their connection with certain processes of disease. Let us now endeavour to trace out some of these subjects more minutely.

It is well known that, on exposure to the air, blood coagulates, and eventually undergoes a form of fermentation termed putrefaction; that is to say, it decomposes in a certain manner. Lister has shown, however, that blood, removed from the body, has no inherent tendency to undergo such a change, a fact substantiated by his observation that, if care be taken to keep the blood totally excluded from the air, no such decomposition occurs. Blood collected in this way will keep in the fluid state and perfectly sweet for an indefinite period. Nor is it the air itself which is competent to induce putrefactive change, but it is that something which may be, and generally is, present in the air, and which has to be removed, destroyed, or influenced so that the blood may be preserved unchanged. Contact of the blood thus kept fresh, with the most minute trace of putrefied blood, suffices to render the whole bad and decomposed.

Some years ago, Professor Tyndall demonstrated that a ray of light passing through a dark chamber is visible only by means of the vibrating motes which float in the air bearing the light, and that, if sufficient time be allowed, these motes will subside perfectly, so that a ray of light is no longer visible in the atmosphere which previously swarmed with these particles. It is to such motes seen in the sunbeam that Pasteur and Tyndall attribute the power to start fermentation, putrefaction, and other processes in infusions of vegetable or animal origin. Some such idea as this has been more or less current in men's minds for ages; but, advancing to so recent a date as 1857, we find the following passage in a work[1] which then attracted considerable attention:—

'It is not improbable that the glittering motes seen in the sunbeam, when it shines through a small aperture into a dark room, consist in part of these otherwise imperceptible eggs or seeds. Light, we know, is the great and universal revelator.'

Professor Tyndall, then, advanced on this hypothesis by showing that the sunbeam owes its visibility to these motes, and, in common with Pasteur, Roberts, and many other earnest workers, he has followed up the study in some detail. The precise methods of investigation pursued by them must be learned from their own papers; here I can only summarise the results to which their application has led.

The ferment matters which exist in the air may be avoided, as we have already seen, by a process of settling; or the air may be filtered through cotton-wool; or any germs therein may be destroyed by strong heating. Air purified in any of these ways is incompetent to set up those peculiar processes of putrefaction, change, and decay which inevitably happen in animal and vegetable matters exposed to air not so purified; and, if this theory be true, these matters can never ferment or putrefy, or allow of the presence of life, until contamination with previously existing germs or life matter has been effected. This is, in fact, the theory of Biogenesis, a doctrine which was ably expounded by Huxley, in his Address to the British Association of 1871, and one which is now almost universally accepted. Its acceptance, however, is not quite universal; and, on the other side, Bastian, who has devoted himself to this question, goes so far as to assert that he has determined the precise conditions under which urine, for instance, can develope life *de novo*. This is the doctrine of Abiogenesis. A particular instance cited by Bastian is refuted by Pasteur; but he is charged by the former investigator with having repeated the observation in a manner which would not present the identical conditions under which he (Bastian) has found life to be generated *de novo*. More recent work by Mr. Dallenger and Dr. Drysdale has revealed the fact that, while certain kinds of monads in a fully developed state are entirely destroyed by exposure to a certain temperature (140° F.), that same temperature, or even a temperature of 300° F., maintained for ten minutes, is insufficient to destroy the undeveloped spores which may be present. Professor Cohn, of Breslau, has found corresponding facts to be true of the *Bacillus subtilis* and its spores. These observations have been applied in explanation of the statements made by Bastian. In justice to this last-named observer, however, we may leave the doctrines of Biogenesis and

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[1] *Life: its Nature.* By L. H. Grindon. 2nd edition, 1857.

Abiogenesis as undecided hitherto, while admitting that the mass of evidence is decidedly in favour of the truth of the former. Roberts writes :—'It seems then to be fairly established that organic matter has no inherent power of generating bacteria and no inherent power of passing into decomposition;' further, 'that bacteria are the actual agents of decomposition;' and lastly, that 'the organisms which appear, as if spontaneously, in decomposing fluids, owe their origin exclusively to parent germs derived from the surrounding media.'

On the basis of the work thus briefly sketched, a germ theory of disease has sprung up, and it is to this matter that we must now direct our attention.

In an address on contagium-vivum with which Dr. Roberts, of Manchester, charmed and instructed his audience at the 1877 Meeting of the British Medical Association, he compared the action of yeast upon saccharine urine and the fermentative agency of *Bacillus subtilis* upon hay infusion, to small-pox, and showed that the fever in a bottle resembles this disease in the following points:—(*a*) a period of incubation intervening between inoculation and the commencement of disturbance; (*b*) a succeeding period of disturbance accompanied by elevation of temperature; (*c*) a subsidence of the disturbance and a return to the normal state. Moreover, fermentation, like small-pox, may take place through direct inoculation or by fortuitous infection through the atmosphere. Dr. Roberts, however, carefully guards himself against suggesting that the enhanced temperature in the fermenting urine is a real analogue of the preternatural fever heat.

The yeast plant and *Bacillus subtilis* are the representatives of a large class of organisms which may be grouped under the generic term of *saprophytes*, and these are the kind of organisms which are found to be associated with infective inflammations and contagious fevers.

Dr. Roberts points out that the doctrine of a contagium-vivum necessitates one of two things; either it is an independent organism (a parasite) which multiplies within the body or upon its surface, or it is a morbid cell, or mass of protoplasm detached from the diseased body and engrafted on the healthy body. This last-cited assumption is but a modification of an old doctrine; it is indistinguishable from the views of Liebig. That chemist, proceeding upon the accepted fact that epidemic diseases can often be traced to putrefactive processes occurring in animal or vegetable matter, stated that the liability of persons to the contagion rested upon the presence in the living body of substances which offer no resistance to the cause of change in form and composition acting on it. He wrote,[1] 'If this substance be a necessary constituent of the body, then the disease must be communicable to all persons; if it be an accidental constituent, then only those persons will be attacked by the disease in whom it is present in the proper quantity, and of the proper composition.'

Liebig contested stubbornly, and with eminent reasoning, for the truth of the chemical theory over that of the parasitic theory of disease, and contended that if any one contagious disease were to be explained, all must be equally explicable. Thus, after writing about scabies, he goes on to say,[2] 'If now we inquire what results the search after the same or similar causes in other contagious diseases has yielded, we obtain for answer that, in the contagion of small-pox, of plague, of syphilis, of scarlet fever, of measles, of typhus, of yellow fever, of dysentery, of gangrene, of hydrophobia, the most conscientious observation has not been able to detect animals, or even organised beings at all, to which the powers of propagation could be ascribed.'

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[1] *Animal Chemistry*, by Baron Liebig; translated by Gregory. Third edition, 1846.

[2] *Ibid.* p. 209.

Even nowadays the advocates of the germ or parasitic theory admit that, as far as typhus, scarlet fever, measles, and the rest of the contagious fevers are concerned, 'their connection with pathogenic organisms is as yet a matter of pure inference' (Roberts).[1] On the other hand, vaccinia, small-pox, sheep-pox, diphtheria, erysipelas, and glanders are stated to have been proved to possess a virus consisting of minute micrococci.

Here it will be best to confine our attention to the three diseases of which Dr. Roberts treated in his Address at Manchester, viz., septicæmia, relapsing and splenic fevers. Let us take, first of all, septicæmia. When wounds become unhealthy, the discharges become offensive and breed organisms, and inasmuch as investigations (already referred to) have shown that bacteria are the acting causes of decomposition, and further, inasmuch as Dr. Burdon-Sanderson and others have shown that decomposed albuminous fluids are poisonous, it is therefore concluded that septicæmia is not only due to organisms, but that such wounds as those referred to, give offensive discharges by virtue of the action of the bacteria in them upon the surrounding albuminous parts.

Now it has been proved again and again, that a healthy subject cannot be infected by means of organisms alone; they cannot live on healthy surfaces or in healthy tissues, or otherwise every inspiration would carry into the blood the first seeds of all kinds of disease; these germs, then, are not the poison, but, under given conditions, by their action upon albuminous matters, they produce the poison. With this knowledge we are asked, on the germ theory, to understand as a consequence the production of septicæmia and pyæmia. Septicæmia, then, is the result of the introduction into unprotected parts of the body, or wounds, of organisms; these act upon the discharge, and produce the septic poison. Surely, this is no parasitic theory; it is the chemical theory of Liebig; the septic poison being that matter which Liebig would say has undergone change by contact with something else previously in course of change.

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[1] See Reports on the *Life History of Contagion*, by Dr. Braidwood and Mr. Vacher.

This poison seems to be particulate, and may be separated, for instance, from decomposed meat infusions by filtration through unglazed porcelain (Burdon-Sanderson, also Panum).[1] Such meat infusions, when introduced into the blood system of animals, produce a simple uncomplicated paroxysm of fever, beginning with a rigor which is succeeded by a rise in temperature, and concluding in defervescence and recovery, if the dose be not too great; if too great, death results. When the particulate poison, or pyrogen, as Dr. Burdon-Sanderson terms it, is first separated by filtration, as described, the filtrates are powerless to induce disease.

These facts are so remarkable that they deserve a little more attention. They are remarkable because the poison does not consist of living matter, nor is it necessarily accompanied by living matter, although it has originally been produced through the agency of bacteria. These experiments were first made by Panum, but more recently have occupied the attention of Dr. Burdon-Sanderson.[1] He prepared his septic solution by precipitating putrilage by alcohol, re-dissolving the precipitate in water, evaporation to dryness, and re-solution of the residue in water. These processes necessarily preclude the absence of all living matter in the product, and yet, in contrast with this fact is the further fact that the putrilage was originally produced through the agency of bacteria in the presence of air and water.

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[1] *Report Medical Officer, Privy Council, &c.* New Series, No. viii.

Further, Hiller has shown that, by washing septic bacteria with pure water, they can be deprived of all toxic properties without injuring their life activity.

Relapsing Fever.—From time to time, spiral organisms (*spirilla*) have been detected in the blood of patients suffering from this disease, the observation having first been made by Dr. Obermeier, of Berlin; they are found during the paroxysms, but are absent at the crises and at the subsequent apyrexial periods. It appears that the fever is easily communicated to a healthy person by inoculation with the blood of a patient suffering from the disease, but only if the blood be taken during the paroxysmal periods; hence it is concluded that the spirilla are the actual virus of relapsing fever. Ocular evidence of such germs (if such they be) is almost entirely wanting, while all attempts to cultivate them out of the body have failed. Here again, therefore, we are dealing more with inferences than with facts.

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[1] See *British Medical Journal* for December 22, 1877, and some subsequent numbers.

Splenic Fever.—In 1855 Pollender discovered minute staff-shaped bacteria in the blood in cases of this disease, and the observation is said to have been often confirmed since. Not only is the germ found in the blood, but also in the spleen, the lymphatic glands, &c., and it is now considered by the advocates of the germ theory, that this particular bacterium is the true virus of splenic fever. It is true that the observations made by Cohn, Burdon-Sanderson, and Koch upon this subject lend some weight to the hypothesis, and Koch appears to have determined that the introduction of such germs into the blood of healthy animals brings on splenic fever. The germ is said to be identical with the *bacillus* of Cohn, but, whatever it is, it has not yet been proved whether the disease is due to the germ directly, or to any altered organic matters brought about by its agency, and anything beyond what has been stated above is the merest speculation.

It is upon such grounds as those brought forward that the doctrine of a contagium-vivum is thought to be established on a solid foundation. Let us put this foundation a little more to the test.

Both Dr. Sanderson and Dr. Klein maintain that, in cases of enteric fever, a luxuriant growth of micrococci may be observed in the diseased intestines. Klein, however, goes further than this, and describes certain fungic forms present in the follicles of such intestines; but what connection these may have with the disease is not precisely determined. Dr. Creighton showed that these so-called fungic structures, in the case of small-pox of sheep, supposed by Klein to consist of mycelium and gonidia, were, in reality, coagulated particles of albumin.

In a more recent paper[1] Dr. Creighton reports on the infectiveness of cancerous tumours, in special reference to infected lymphatic glands. In surgery, such growths are termed 'malignant,' and they arise in lymph glands when cancer, operating from some spot in which it has been of primary occurrence, secondarily spreads its infection to them. Dr. Creighton's report of 1874 pointed to the conclusion that the elements of the originally diseased parts have in them a specific ferment-power, which, when carried by lymph or blood-streams to other parts, impregnates these, and the tumour grows out of the original textural type. This opinion is confirmed in the latter report, and is in opposition to the idea of a germ power. In this way a part affected by tumour is supposed to consist of the same matter as before infection; only, by virtue of an induction (communicated by a ferment-power) to grow in a new way, it does so.

Taking, therefore, a general survey, it cannot be fairly said that the parasitic theory, as ordinarily explained, is explained correctly. The grounds upon which this theory is based are indisputable, but there is an almost universal tendency exhibited to exceed the legitimate inferences to be made from them. This fascination has led many into error, and in it is to be found the origin of what may be called public 'scares.' Thus, of late years, an attempt has been made to connect the causes of typhoid fever with impure milk, containing, as it is supposed, virus matter derived from sewage or other effete substances.

The same explanation has been made in regard to recent outbreaks of scarlet fever. Quite lately[2] an epidemic of this kind raged at New Barnet, 'and was apparently caused by infected food, in this instance presumably milk.' It was endeavoured to prove this in the old way, namely, by first of all assuming the milk to be the real cause, and then showing that most of the sufferers were supplied by the same milk vendor. Such a method is as illogical as the attempt to find out the true cause is commendable. The total number of cases which happened during the two months was 140, and of these 131 were supplied with the same milk. This fact lends some plausibility, at first sight, to the theory in question, but, on further study, this disappears. The 131 cases occurred in 58 houses, but the same milk was supplied to 77 houses in which there was no fever. Further, nine cases of fever occurred in houses supplied by other milk-vendors. It is thus seen that the one particular dealer whose milk was suspected had practically a monopoly of the trade, and assuming the outbreak—without regard to its cause—to have commenced in his district, it would follow as a matter of course that the disease should be chiefly confined to that location. It hence appears there is no safe foundation, or even plausibility, for assuming that milk was here, or ever has been, the originating cause, or the propagating agent, of scarlet fever or any other disease.

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[1] *Reports of the Medical Officer of the Privy Council.* New Series, November 1877.

[2] See *Practitioner*, October 1877.

Let me be understood distinctly in this statement. I do not intend to convey the notion that there can be no truth in the germ theory of disease, but merely to point out that, hitherto, no absolute proof of its truth has been advanced. Even supposing, in the matter of the scarlet fever epidemic, to which allusion has been made, it could be demonstrated that the suspected milk is capable of communicating the disease when injected into the blood of a healthy person (and this has not yet been done), it would still remain to be proved which ingredient of the milk constitutes the virus. We have seen that various forms of bacteria may be introduced into the blood with impunity, may be inspired in every breath, and conveyed into the stomach with all kinds of food, and yet no disease results; but now and then outbreaks of disease occur, and the origin is traced, with more or less probability of truth, to decomposed putrescent matter. Surely all this does not point to a germ theory of disease, as ordinarily understood, but rather to a chemical theory like that maintained by Liebig. In this case germs are merely the concomitants of disease.

Mr. W. Stewart appears to be guided by such views in a paper[1] which recently appeared, on the subject of 'Typhoid Fever.' He gives facts which induce him to believe that this disease is caused by the reception in the system of decomposing albuminous matter, which may have been derived from blood, or the liquid evacuations in diarrhœa, in which cases it may be remarked that much albumin is held in solution and has been originally derived from blood serum. This theory is sustained, perhaps, to some extent by some recent experiments of M. V. Feltz, which consisted in injecting a solution containing in suspension dried putrid blood into the crural veins of dogs. In all instances symptoms were induced and effects caused, resembling those occurring in typhoid fever. Trustworthy or untrustworthy, we have here at least something tangible and which does not defy study, the further investigation of which might throw some valuable light upon the processes in question.

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[1] *British Medical Journal*, March 10, 1877.

To revert now to another part of the subject. Pasteur claims to have demonstrated that every kind of fermentation is accompanied by the reproduction of the ferments, and that these in all cases consist of low forms of life. Whether, however, each kind of fermentation has its own special ferment, as for instance is the case with the lactic and alcoholic fermentations, is vague and uncertain. In reference also to putrefaction, it is considered that Pasteur has proved the same thing to be true, in spite of the contending views previously held. He, however, distinguishes two kinds of putrefaction, viz., that in which the ferment (as, for instance, the butyric ferment) produces the change without the aid of oxygen, and that in which oxygen is also essential in promoting such change. To confine ourselves for the moment to the first of these.

When putrescible solutions are exposed to the air, there forms on the surface a film of bacteria, mucors, and mucidines, which are supposed to exclude and absorb oxygen, preventing it from penetrating into the liquids. Under the film in the liquid, vibriones multiply and split up the albuminous substances into simpler products, while the bacteria and mucors excite their slow combustion into ultimate products. This is M. Pasteur's view of the phenomena of putrefaction, and it should be noticed that vibriones cannot endure the presence of oxygen; their function is the institution of initial change, which is completed by the bacteria and mucors. One thing is, however, necessary for this action of the vibriones to occur, viz., the presence of water. Now, so far as has been ascertained, the first products of change above alluded to are identical with those which result in the laboratory when albuminous bodies are subjected to decomposition by hydration, that is to say, by water at high temperatures, or by boiling with such reagents as sulphuric acid, potash, or baryta. The ultimate products produced in putrefaction are those which result in the laboratory when these others are further subjected to oxidising influences.

M. Donné states[1] that, when eggs contained in the shell are broken up by shaking, and then protected from the air by coating the shells with collodion, they still putrefy in process of time, while the most scrupulous examinations will detect no form of life whatever among the products. These observations are supported by M. Béchamp. On the other hand, M. U. Gazon concludes[2] from an investigation, that 'putrefaction in eggs, whether in the presence or the absence of air, is correlative to the development of and multiplication of microscopical organisms of the family of vibriones.'

These opposed statements, as also others of a like kind, should make us careful in accepting Pasteur's theory to be universally correct. Assuming, however, that it is correct, we may reduce the phenomena of putrefaction to a few issues, which in their ultimate meaning remain true, even if Pasteur's theory shall be eventually disproved.

Albuminous matters have no inherent tendency to change, and they may be protected from change by suitable means; but, inasmuch as they are possessed of large molecular proportions, the impulse required to break them down into simpler products is not great; when once decomposed to this extent, these simpler bodies are resolved, under suitable conditions, into ultimate products. Take, for instance, blood serum and expose it to the air, and what happens may be assumed to be somewhat as follows:—

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[1] 'Experiénces sur l'Altération Spontanée des Œufs.' *Compt. Rend.* lvii. p. 450 (1863).

[2] Paris, 1875. *Faculté des Sciences de Paris,* No. 362. Thesis for the Doctorat ès Sciences.

A vibrione falls into the liquid, and by feeding in a medium suitable for its development and propagation, it thrives; incidentally, the albuminous molecule is split up, just as the liver has the power of splitting it up to make bile, or as the blood seizes oxygen in the lungs and rejects the nitrogen. This life act of the vibrione is that impulse requisite for the decomposition of the albumin, the body in change, as Liebig would put it, capable of setting another body—in this case the albumin—with which it is in contact, also in a state of change. Then other forms of microscopical life introduce themselves, and assist the decomposition similarly, the whole being supplemented by further changes induced by the presence of air and water. It is even conceivable that the very life act of the vibrione is one of hydration, that is, one which determines the assimilation by the albumin of the elements of water, just as baryta water or dilute sulphuric acid would do it also under other conditions. But whether this be so or not, the vibrione, if it be the cause of change, is only on a par with other causes of change. Further, the vibrione, if transplanted into the animal economy, will not produce disease so far as is known, yet the putrid blood serum produced by its agency will do so. What is the inference? Simply this. That germs do not constitute *contagium* itself; they have a capability of action sufficient under given conditions to produce that *contagium*, but they themselves are not the germs of disease.

Hitherto attention has been confined almost entirely to living germs; there is, however, another class of ferments, the chief characters of which may be briefly given here. Thus, we have the ferment which is capable of splitting up cane sugar (before it is fermented into alcohol) into glucose and lævulose; the emulsine of almonds, and diastase; the ptyaline of saliva which transforms starch into sugar, and the ferments of the spleen and pancreas which exercise a similar chemical function. These soluble ferments, or *zymases*, appear to be derivatives of albumin, but are in no sense possessed of vitality, and therefore do not reproduce themselves in the changes in which they are concerned. Moreover, in most cases, similar reactions (and leading to the same results) may be induced by many inorganic substances, such as acids and alkalies; in fact, the action of soluble ferments may be expressed as one of hydration. Of all bodies liable to change, the most complex in constitution are the easiest to succumb to influences of this kind. Liebig writes:[1]—'In fact, the larger the number of single elements and atoms which have united to form a group of atoms of definite properties, the more multifarious the directions of their attractions, the smaller must be the force of attraction between any given two or three of the atoms. They oppose to the causes of change in form or composition acting on them, such as heat and chemical affinity, a far less resistance, they are far more easily altered and decomposed, than substances of a less complex composition.'

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[1] *Animal Chemistry*, part i., English edition, 1857, p. 196.

Now it has been pointed out that, so far as the products resulting from the putrefaction of albumin have been identified, they are identical with those induced by processes of hydration. Unfortunately, this knowledge is not very great, although the subject has been studied by Braconnot, Erlenmeyer, Schaeffer, Habermann, Nasse, and more particularly, by Schützenberger. It is impossible, in this place, to consider this subject any further in detail, but our present knowledge may be thus summarised. The albuminous principles, though many in number, seem all to be referable to a common type, just as the various fats are, and that when these are subjected to those processes which, when applied to fats, determine their decomposition into glycerine and fatty acids, they are also decomposed first into substances few in number, but of altered properties, although not far removed from the parent molecule, while, finally, these intermediate substances are resolved into urea and amidated acids of various series. The institution, then, of putrefactive change, is simultaneous with the appearance of these products; and, some time ago, I occupied myself with many experiments upon this subject which were necessarily cut short by unavoidable circumstances. I hope, however, in the future to be able to follow out certain indications which I then obtained, that the pursuit of this particular chemical method promises to throw much light upon the true chemistry of infection, for there can be no doubt that, sometimes at least, an infectant is a non-living product of the decomposition of albumin, and one which may perhaps be expressed by a chemical formula.

It is true Bergmann has stated that septic poison may be produced without the presence of any albuminous compound. Indeed, he states that he grew bacteria in a liquid containing sugar, ammonium tartrate, and inorganic salts, and found that while the first crops were inert, the ultimate particulate liquid constituted a virulent poison. It is more than probable, however, that bacteria themselves have an albuminous structure, and that their life depends upon the construction of new tissue from the media in which they live. In other words, that as by their life act they perform, it may be, the synthesis of albumin, so by other acts of life in which the tissue is broken down, they throw off the products of its decomposition.

Antiseptics.—An antiseptic is a body which, by its presence, protects matters from those specific decompositions which in a collective sense we term putrefaction, while a disinfectant is, properly speaking, a substance which will take from the infectant matter, when formed, its specific characters and render it harmless. It is quite immaterial therefore, whether agents employed for these purposes be germicides or not; that is to say, the qualification of an antiseptic is not necessarily the possession by it of the power of killing germs, but rather the possession of the power of preventing these same germs or other causes from initiating those processes in decomposable matters which we term 'putrefaction.' Hence it was that, when, some time ago, I discovered a solution for which I claimed these antiseptic and disinfecting powers, I insisted so strongly on its importance. This solution, popularly known as 'Sanitas,' contains camphoric acid, peroxide of hydrogen, and certain other camphoraceous ingredients; curiously enough, among these latter is a substance very similar to thymol in its character. So far as my later experiments go, I have not been able to satisfy myself whether the thymol-like body has the composition $C_{10}H_{14}O$ or $C_{10}H_{16}O$, but that it has an intimate chemical relationship to that substance, and is possessed of similar antiseptic powers, there is no doubt. This fact is the more interesting because Bucholtz has recommended thymol as a very powerful germicide, and hence it is not difficult to perceive that the presence of a similar substance in 'Sanitas,' together with the other constituents, sufficiently explains the antiseptic and disinfecting characters of this solution.

As is well known, this solution is produced by the action of air upon turpentine in the presence of water. In fact it consists of an aqueous solution of the aerial oxidation products of turpentine, and it, among all other available antiseptics and disinfectants, alone possesses those other characters which must be demanded of a protective agent to be employed by the mass of people, —that is to say, it is non-poisonous, and without harm to metals, clothing, and furniture. By immersing such decomposable matters as fish and meat in 'Sanitas,' or by spraying them at regular intervals with the solution, it is possible to preserve them almost indefinitely. Tainted foods admit of restoration to sweetness by the same treatment.

I have also substantiated the antiseptic character of this fluid in the way already indicated, viz., by searching in matters preserved by 'Sanitas' for those particular chemical products which always accompany the decomposition of albuminous substances, and so long as they have been thus preserved, these products, including tyrosine, leucine, aspartic and glutamic acid, &c., have never been detected by me. In other words, by proper disposition of this fluid, the formation of putrilage may be averted, and in so doing the production of septic poisons or infectants is consequently avoided.

Of other antiseptics or disinfectants it is unnecessary to write at any length, because while their action is familiar to most persons, we have but little information regarding the specific manner in which, individually, they act. For a more detailed account of the manner in which they are supposed to act, we may refer the reader to certain well-known works upon such subjects, particularly to Schützenberger's treatise on Fermentation.[1] Here we may conclude with a few remarks upon the better known substances available in everyday life.

Among antiseptics some are supposed to act by virtue of their attraction for water, as, for instance, alcohol and common salt.

Other bodies, again, actually combine with the decomposable substance, and the combinations thus formed are too strong for the dissociating influences to break them down. Sulphurous acid and bisulphites are supposed to act in this way.

Oils, fatty matters, sand, ashes, &c., act often as antiseptics by behaving as filtering matters which retain the germs contained in the air or wafted by it, and which, unless kept back, would cause putrefaction in the matters desired to be preserved. Thus these substances act like cotton wool in the antiseptic treatment of wounds.

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[1] *On Fermentation*, by P. Schützenberger. H. S. King & Co., London.

The function of carbolic acid applied to albuminous matters has been conjectured to consist in its power of coagulating the albumins, which in this state are not so liable to change. It is also claimed for carbolic acid that, like thymol, it actually kills the low forms of life which induce putrefaction in suitable matters; in other words, it is a germicide. Unfortunately, however, those agents which behave as germicides are also more or less poisonous to man, while carbolic acid, moreover, is not a pleasant agent to employ. Salicylic acid and a number of other bodies behave like carbolic acid, but are attended with certain difficulties as regards their use. Moreover, they are not disinfectants in the proper sense of that word.

Substances like permanganate of potash often act by destroying the matters which would otherwise putrefy or have putrified, but more often they merely oxidise volatile compounds which have a bad smell, and it is too often imagined that when the smell is removed the danger is abolished. This, however, by no means necessarily follows.

CHAPTER XXIII.

THE PHYSIOLOGICAL ACTION OF CHEMICAL SUBSTANCES.

THAT many chemical substances have a distinct physiological effect upon the human body has been known for ages, and perhaps the most familiar instances that can be adduced in the present day relate to chloroform and chloral, both of which bodies were discovered by Liebig. It is not desirable to describe at any length the virtue of the first of these reagents for obviating pain, and that of the second one for inducing sleep; and indeed, although the virtues might be extolled, but little explanation could be attempted. It is certainly known that both are the results of reaction upon brain or nerve matter, but the precise nature of those reactions is a question from the solution of which we are perhaps as far removed as from any ultimatum in science. The two substances to which allusion has been made, stand by no means alone, and already in a former chapter the physiological action of ordinary alcohol has been described so far as it is at present known.

In 1868 Dr. A. Crum-Brown, F.R.C.P., communicated to the Pharmaceutical Meeting at Edinburgh a paper on 'Chemical Constitution, and its relation to Physiological Action,'[1] in which, for the first time, this study was reduced to something like scientific rule. It was then pointed out that the soluble compounds of a poisonous metal like lead have nearly all the same action, but that although arsenic is poisonous, a readily soluble organic combination containing this metal—kakodylic acid—is perfectly inert. Again, while cyanogen is poisonous, a number of compounds, as for instance ferrocyanide of potassium, exhibit no trace of the action of hydrocyanic acid.

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[1] *Pharm. Journ.* May 1868.

Stahlschmidt had previously made experiments with methyl-strychnium salts on rabbits, and had arrived at the conclusion that they were quite inert. But Crum-Brown and Fraser[1] showed that this was not perfectly correct; the statement is correct so far as these substances are concerned when administered by the stomach (to rabbits), but when injected subcutaneously, very much smaller quantities give rise to effects terminating in death. These effects are not like those of ordinary strychnia poisoning, viz., tetanic convulsions, but rather represent a condition of general paralysis.

It was further shown that strychnia produces tetanic convulsions by exciting the nerve centres in the spinal chord, but the methyl and ethyl substitution products derived from strychnia produce paralysis by a destruction of the power of the terminations of the motor nerves to receive the stimulus and transmit it to the muscles. Similar differences between various other alkaloids which act like strychnia and their substitution products of the same order, were also observed by Crum-Brown and Fraser.

The great feature in their work was the establishment of a distinct connection between chemical constitution and physiological action.

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[1] See paper read before Royal Society of Edinburgh, January 6, 1868

The physiological action of morphine, narceine, narcotine, codeine, brucine, nicotine, atropine, hyoscyamine, physostigmine, muscarine, veratrine, aconitine, digitaline, santonine, ergotine, and quinine, have also been carefully studied.

Dr. B. W. Richardson has further investigated the action of homologous series of alcohols and ethers.

Here, perhaps, it is important to reiterate that the physiological action of substances varies according to the mode of administration, that is, according to whether they are supplied through the stomach, or injected subcutaneously. It is, however, to the line of research indicated by Crum-Brown and Fraser that it is desirable to direct attention more particularly.

Messrs. J. G. M'Kendrick & Dewar have experimented on the physiological action of certain bases (of the so-called chinoline and pyridine homologous series) which may be obtained from quinine and similar bodies by distillation with potash. When these bases are injected subcutaneously, they act exclusively upon nerve and brain matter, and among the very interesting results obtained, we may note one particularly.[1] 'On comparing the action of such bases as C_9H_7N (chinoline) with $C_9H_{13}N$ (parvoline), or $C_8H_{11}N$ (collidine) with $C_8H_{15}N$ (conia from hemlock), or $C_{10}H_{10}N_2$ (dipyridine) with $C_{10}H_{14}N_2$ (nicotine from tobacco), it is to be observed that, apart from difference in chemical structure, the physiological activity of the substance is greater in those bases containing the larger amount of hydrogen.' Of course this conclusion, given in the words of Messrs. M'Kendrick and Dewar, only expresses the facts observed; and while its interest is exceedingly great, we must not be carried away to make generalisations which require much more work to be definitely established. Above all things, it is desirable to ascertain what becomes of the bases thus subcutaneously injected, and the precise manner in which they act on the brain and nerves; it is not sufficient to be acquainted merely with the channel through which they act. The difficulty presented, however, in such studies is enormous. One grain of some of these bases per pound of body weight (for rabbits) is sufficient to cause death, and it is quite impossible, in the present state of science, to trace such a small quantity of substance through the system, and still more impossible to ascertain its precise mode of action; we can at present only ascertain the most prominent results as they are revealed to us.

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[1] *Proc. Roy. Soc.* vol xxiii. p. 297.

Professor M'Kendrick has continued this study in conjunction with Dr. W. Ramsay.[1] They find that pyridine, picoline, and lutidine, and their salts, only produce drowsiness, but the methyl iodides of these bases are powerful irritants to the cerebral centres and produce paralysis of the fore limbs. The ethyl and allyl derivatives act similarly, but more intensely.

Dipyridine and dipicoline produce the same effect, only more strongly; but when combined with methyl or ethyl iodide, they constitute fearful poisons.

The ammonium salt of dicarbopyridenic acid produces fits resembling epilepsy, but its methyl ether had no appreciable effect.

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[1] *Phil. Mag.* Oct. 1877; see also *British Medical Journal*, May 4, 1878.

While, therefore, as a rule the physiological action of substances seems to become more intense as the molecular complication increases, the effects largely depend on the specific character of the individual substances.

In connection with a similar subject, Prof. Gamgee, of Owens College, and some of his pupils, communicated to the British Association Meeting at Glasgow (1876) several investigations which are of interest. They relate to the action of various compounds of vanadium, of chromium salts, and on the differences presented in the physiological actions of ortho-, meta-, and pyro-phosphoric acids. The general results thus attained may be expressed as follows:—

(*a*) The physiological action is in part dependent upon the number of atoms in the molecule and its complexity of structure.

(*b*) Also upon the degree of stability of the molecule.

The more complex the molecule, the more intense and prolonged is its action, and if the substance be peculiarly liable to split up into simpler compounds, it will act more intensely than otherwise. It is needless to state how purely tentative are such generalisations. In fact, in my opinion, it would be best to reserve such generalisations, and be content with the facts until our knowledge has attained more precise and less misunderstandable results.

In his Address to the Department of Anatomy and Physiology at Glasgow,[1] Dr. J. G. M'Kendrick warned investigators against pursuing such inquiries as these in a haphazard sort of way, 'with the vague hope of coming upon something new,' and pointed out how essential it is [illegible] success that investigators should take up such [illegible] continue them in the light afforded by previous researches. It is true that now and then a valuable therapeutic remedy is discovered, quite accidentally as it were, but after all, such an isolated result is not of a value comparable to that which must attend a general understanding of the laws which regulate the connection of chemical structure with the physiological effects of substances.

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[1] British Association, 1876 (John Greig & Son, Edinburgh).

We shall conclude this chapter with a brief summary of two lectures[1] given by Prof. Emerson Reynolds upon the subject here under description.

All chemical substances introduced into the body act upon it either physically or chemically. The physical effect is one which may be produced without an attendant change of composition in the agent employed or those parts of the body which are acted upon. The chemical effect is one which is attended by a change in composition of the substances alluded to. But of course some bodies act both chemically and physically. Unsaturated compounds, or compounds whose power of combination is [illegible] are the most energetic in their chemical [illegible] among such bodies that those which [illegible] physiological action occur.

[illegible] reduces the known facts of the study to [illegible] The first of these asserts 'that bodies [illegible] same elements in the same proportions [illegible] in physiological activity when com-[illegible] favourable conditions; and that the observed dissimilarity in action is due to difference in chemical constitution.' He instances this by the following case: cyanide of methyl, CH_3CN, or carbamine, is metameric with another substance (producible in the same reaction) termed a *nitrile*, which is of the same composition but different in constitution. The nitrile is almost destitute of physiological action, while the carbamine is a powerful poison. Dr. Reynolds explains this case by assuming, upon the purely chemical grounds that in the carbamine the carbon has only two of its bonds satisfied, and two bonds of the nitrogen are also unsatisfied, whereas in the nitrile the carbon bonds are fully satisfied, and only the two nitrogen bonds are latent or self-combined. This is better seen by using the developed formulæ of the two substances:—

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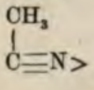
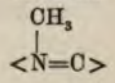
[1] [illegible] Medical Science, or *Pharm. Journ.* July 21 and 28, [illegible]

Nitrile.



$$\begin{array}{l} CH_3 \\ | \\ C\equiv N> \end{array}$$

Carbamine.

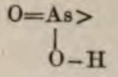


$$\begin{array}{c} CH_3 \\ | \\ <N=C> \end{array}$$

The second proposition asserts that 'groups of bodies exist which contain the same elements in different proportions and are similar in chemical structure, but which differ materially in degree of physiological activity.' This proposition is substantiated by the work of Messrs. Gamgee, Priestley, and Larmuth, previously referred to. Sodic orthophosphate (Na_3PO_4) is almost inert, while the pyrophosphate ($Na_4P_2O_7$) is an energetic poison; the metaphosphate ($NaPO_3$) is also poisonous, but less active than the pyrophosphate. The physiological activity of the pyro- and meta-phosphates is attributed to the liability they exhibit to pass into the orthophosphate under conditions which may reasonably be supposed to obtain in the body. Larmuth has further shown that in the group of sodic vanadates the order of activity is the same as that existing among the phosphates.

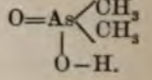
In further illustration of the proposition before us, we may again refer to what has been already stated, viz., that kakodylic acid containing 54 per cent. of arsenic is physiologically inert, while arsenious acid is a deadly poison. Their similarity in structure is exhibited by the formulæ :—

Arsenious Acid.



$$\begin{array}{l} O{=}As> \\ \;\;\;\;| \\ \;\;\;O{-}H \end{array}$$

Kakodylic Acid.



$$\begin{array}{l} O{=}As\begin{smallmatrix}\diagup CH_3 \\ \diagdown CH_3\end{smallmatrix} \\ \;\;\;\;| \\ \;\;\;O{-}H. \end{array}$$

Again, the researches of Beaumetz and Audigé, as well as those of Dr. B. W. Richardson, furnish another illustration of the proposition we are considering. The two former observers conclude that the lethal dose of certain of the alcohols per pound weight of animal is approximately :—

42 grains of ethylic alcohol	C_2H_6O
33 „ „ propylic „	C_3H_8O
13 „ „ butylic „	$C_4H_{10}O$
5 „ „ amylic „	$C_5H_{12}O$

That is to say, the higher we go in the series the greater is the degree of physiological activity. There appears, however, to be one exception, viz., that methyl alcohol, CH_4O—the lowest member of the series—is, according to Beaumetz, more active than ethylic alcohol.

From certain considerations, Rabuteau was led to conclude that the physiological activity of an element increases with the atomic weight, and to a certain extent this appears to be true, although it cannot be accepted as universally true. From what is known of the action of the meta-nitrate, meta-phosphate, meta-vanadate, and meta-arsenate of sodium, the physiological activity of the characteristic elements, viz., nitrogen, phosphorus, vanadium, and arsenic, seems to be in the same order as that of their atomic weights.

The third proposition of Dr. Reynolds is as follows: 'bodies which are unlike in composition, but which agree in being either actually or constructively unsaturated, and are alike in certain marked chemical relations, often agree in physiological action.' Thus both phosphorus and pyrogallic acid ($C_6H_3(OH)_3$) are both characterised by the property of a strong affinity for oxygen, and both act, according to Personne, in the same way in the animal organism. Phosphorus is actively unsaturated, whilst pyrogallic acid is constructively unsaturated.

The fourth proposition asserts that 'the result of chemical addition to unsaturated molecules is either to destroy or to materially modify their physiological activity.' This statement is supported by the work of Crum-Brown and Fraser, and the researches of Messrs. M'Kendrick, Dewar, and Ramsay, already described. Professor Schroff, of Vienna, has also indicated similar facts.

Dr. Reynolds concludes his lectures by describing the chief ways in which most chemically and physiologically active bodies act in the organism.

(1) By the direct removal of oxygen from the blood, and consequent interference of the process of oxidation.

(2) By combination with the colouring matter of the blood, and consequent interference with its functions as a carrier of oxygen.

(3) By combination with effete materials, thus increasing the difficulty of its removal from the body.

(4) By withdrawal from the living tissues of matters essential to their healthy functions.

(5) By combination with living tissue, and consequent interference of normal functions.

As it is possible by our knowledge of the nature and properties of substances to predict in some measure their action one upon the other, and in fact to foretell their next states, so the same holds good when the substances entering into the composition of the animal body form one side or both sides of the equation. Hydrochloric acid acts upon chalk with the evolution of carbonic acid, and it matters not whether it happens in a beaker or in the human stomach, only the one reaction is regarded as a chemical one, and the other too often as a purely physiological one. This may be stated in another way. Granted sufficient knowledge of two bodies, and securing the contact of those substances, it is possible sometimes to predict the result. If one of those substances happens to form part of the brain, or liver, or lung tissue, then if the other substance be swallowed and come into contact with it, the same result will ensue to a certain extent. The retarding influence of vital force (as we are pleased to call it) arises from the state of combination already possessed by substances forming part of the human body, and any experiments which physiologists may perform, having reference to the physiological action of chemical substances, can only result in a more or less imperfect knowledge of this retarding influence. Even when that is known, it cannot be considered an absolute guidance, because in the first place the action of any substance, be it physical or chemical, is very difficult to localise, and a knowledge of the affected parts is equally difficult to ascertain; and then, after all, the composition of the substances so affected is at the best but very imperfectly known. Above and beyond all other matters affecting health and disease and a knowledge of life, a greater acquaintance with pure animal chemistry is necessitated. In what has preceded it has been attempted only to indicate the connection of chemical constitution with physiological action. Those who may desire to make themselves acquainted with the general therapeutic actions of drugs will find a concise account in the work[1] by Burness and Mavor, to which we must refer them.

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[1] Baillière, Tindall, and Cox, 1874.

CHAPTER XXIV.

CHARACTER.

CHARACTER is almost universally regarded as something apart from the body of man himself; something for which each man is individually responsible; something which, born with man, is developed and cultured into maturity by education and training, be that mature state one for evil or one for good. Yet what, people ask, has this or that man's character to do with his mere animal body? surely character, it is said, forms part of the mind, which, while it associates with the body is yet distinct from it; it is that part of the man which outlives his body and passes away to a future state, real though unseen, realisable only in death. But such inquiries do not envelope the real points at issue; are not deep enough to satisfy even common sense, and, after all, common sense is the best logic. Let first causes be what they may, and so also let us hide our face from the infinite future, and regard man as an intelligent machine complete so far in himself. As the steam engine is a machine for purposes of locomotion, and as the spinner's wheel is a machine which gathers into its vortex and arranges therein, in definite order and beauty, a thousand threads and a thousand tints, so man also is a machine. A machine is he which thinks, speaks, and acts; it is only in the first of these functions that he differs materially from other machines; it is by the acts of a man that he is judged. Upon a knowledge of such acts, mankind ascends the tribunal and pronounces upon character. Nevertheless, inasmuch as acts are pre-determined by thoughts, these should rather form the basis of judgment, where judgment is necessary. But alas, who can know the thoughts of another; 'the heart knoweth its own bitterness' only. And thus man never understands his fellow man aright; he picks out a few crystalline threads of an individuality; he sees a few bright or black bands in the spectrum of his neighbour's life, and without touching the colloid mass which will not crystallise, and being blinded to those parts of the spectrum which are not revealed, man judges his fellow.

Is it not possible then to reduce man to the common level of inorganic matter; to regard him as a mass of matter of mixed chemical constitution, in which thoughts, words, and deeds are but part of the other side of the equation? On this side we have the gross matter in process of continual change; on that side we have the changed matters and those life acts which balance the original matter and the forces which operating upon it caused the change to occur.

Liebig taught that every thought occurring to a man was equivalent to the destruction of a brain cell; this, however, is not the case. The brain seems rather to be a receptacle for those currents, be they electric or not, which are generated by the oxidation occurring in the blood. These currents of force are conveyed by the blood corpuscles, perhaps, to the brain and stored therein. From thence it is transmitted through the nervous system to all parts of the body, and thereby the muscles are regulated in their movements, the organs governed in their different functions and capacity, and life kept going. But what is thought? Physically considered it must be part of that same blood-generated force which becomes metamorphosed by contact with cerebral matter or by some other influence. At least it is an entity, and has its equivalent in inorganic matter and physical force. A man who thinks much grows hungry, just in the same way as a man who works hard grows hungry, and for the same reason. In both cases the force which in our imperfect knowledge we qualify vital, becomes used up below par, and to keep it in sufficient quantity we must eat, have a greater oxidation going on in the blood, and an increased amount of force stored in the brain.

In short, man is a cerebrating creature, as the cow is a ruminating creature. The cow goes on eating grass because it is its nature to eat grass, and it can do nothing else except move. So man can only eat, move, and cerebrate. He cannot help cerebrating, and the degree in which he thinks and thinks well, is the degree of his intelligence, by which his movements are governed. When this intelligence is naturally very large it is called 'genius.' We can conceive a man who is blest with a good digestion, excellent lungs, and well-formed brain cells to be a 'genius,' in the sense that, with proper education and supply of facts, he can arrange those facts into systems, propound generalisations, and make forecastings. But supposing those brain cells are not well formed—are abnormal either in anatomical structure or in chemical composition—what then? Well, his lungs and digestion may be ever so good, but the excessive force generated in the blood is only converted in that case into muscular power; the man is either a splendid 'hitter' at cricket, or 'pulls' magnificently at an oar; and it is quite true that brain cells do differ in form and composition, just in a similar sort of way as lungs and hearts differ. The admired intellect of a nation is often cut off by lung disease at an unripe age, while the fool may grow a snow-white beard!

Thus man is no doubt the creature of circumstance; but he is not alone the creature, he is also the creator. He can intervene between events and divert their original courses; the degree in which he can do this, or does it, is a part measure of his intellect and his energy.

Can, then, a man be held responsible for his actions? To this we answer yes, and no. We have seen that there is a predetermining influence in the very fœtus of man; the protoplasmic mass being endowed with powers of selection and growth in particular ways. Man, the result, steps on to the platform of life, in some measure at least as an automaton. He is born of others, and finds himself with a head upon his shoulders, but the quantity and quality of brain matter in the head is not ordained of himself. He may be a genius; but, horror! he may prove a fool! No doubt the recipient faculty of man empowers him to modify and qualify his creeds, his words, and his deeds; but the first quantity can never be left out of consideration, in spite of all the efforts made in the way of diet, education, and cultivation, to improve.

As the natural state of men is not uniform, all men are abnormal one to the other, for there is no one who can be picked out from the rest and of whom it can be said, this is the standard of men. In the same way as abnormality is but a mild declension of normality, so pathology is but an intensified declension of normality. The governing forces suffer in direction or intensity, and abnormality results; it may be of mind or of body, or sadder yet, of both. Thus even mundane chemical science has a part to play in the *rôle* of what poor mortals call their souls; it has something to do with every poeism originating in the mind of the poet, with every transcendant hope of the philosopher, with the logic of a Mill, and the teeming intelligence of all. A man is suffering, say, from softening of the brain, and yet his intellect is unimpaired, although surely he may be hastening to the grave. How is this? Merely because that particular part of the brain—if such part there be—which transforms the blood-oxidation force into thought is not affected. But search further, and it is found that another part of the brain is affected, the lecithine being decomposed into glycerophosphoric acid, fatty acids, and neurine, and as a consequence the man's volition suffers. Henceforth he cannot be held accountable for his acts so far as these are governed by his will, for his will has suffered through a breaking up of those very brain cells upon the wholesome structure of which the health of his volition depended.

Yet these some brain cells, one and all, the whole body itself, mind and soul, have been elaborated from dead inorganic matter, from vulgar food. After all, perhaps, the epicure is not so despicable; eat, drink, and be merry, for verily that which we eat and drink takes part in that with which we think!

The all-profound mystery of man's mind is wrapped up in the protoplasm of life, with its selective power of construction and reconstruction, of growth and development. Prohibit nutriment, and the protoplasm becomes but as dust of the earth, and yet it circumvests a power none can comprehend. Here is the beginning of intelligence, here is life, and here the hand of God is revealed. None the less, however, when scientifically considered, is it true that man's history amounts to a sort of dynamical expression of the atomic forces resident in and operating upon the very substance of which his body is composed.

CHAPTER XXV.

SHOWING HOW ANIMAL CHEMISTRY MIGHT BE ADVANCED.

It is not intended in this place to develope a complete scheme for the proper advancement of Animal Chemistry, but merely to indicate what can be done in this direction with the appliances ready to hand. Most of the hospitals throughout the country are in some sort of connection with educational schools boasting a laboratory and a chemical staff. Where this is not the case, it would be a comparatively easy matter to institute laboratories and find teachers and workers. These latter should be not only learned in pure chemistry, but also thoroughly acquainted with that branch of the science treated of in this volume. Of course some time would necessarily elapse before such a state of things could be got into thorough working order, and not least because the chemists would have to qualify themselves by proper and prolonged studies for the task of working out questions in physiological and pathological chemistry, and for imparting such knowledge to the students under them.

Assuming this to be not only possible but even accomplished, then a plan of teaching and prosecution of research in physiological chemistry should be adopted in every such institution, and further, the hospitals should provide the laboratories with all important pathological specimens upon which research should also be regularly conducted. In this way, without anything like a revolutionary change in the existing state of things, a vast advance would be possible in Animal Chemistry—an advance which would undoubtedly and speedily be followed by a corresponding movement in pure medicine.

The publication of the researches conducted as above described might be undertaken by a learned society, having for its members, men actually employed in such work; in which case, side by side with other scientific journals, there would be a 'Journal of Research in Animal Chemistry.'

With such a system kept in proper control and health, the face of medicine would be entirely changed in the course of a few years—changed from an accumulation of experiences into a beautiful science.

It would be matter of extreme ease to indicate many of the problems in Animal Chemistry which particularly call for investigation, and below a few of these are given.

Suggested Matters for Research.

(1) The chemical composition and formula of ptyaline; its chemical relationship to albumin; a proper explanation of its ferment-power, and a better study of its general nature.

(2) More complete and exact analyses of the various salivary secretions.

(3) The chemical characters and composition of saliva in disease, particularly in rabies.

(4) The percentage composition of gastric juice unmixed with saliva and food.

(5) The exact composition of pepsin, and the particular changes (if any) it undergoes during the exercise of its digestive action.

(6) General and precise information regarding peptones.

(7) An explanation of the oft-recurring deposition of biliary matters near the pyloric end of the stomach.

(8) General information about the pathology of the gastric process.

(9) The chemical nature of the undetermined constituents of bile.

(10) A better knowlege of the various functions of the bile.

(11) The determination of the destiny of the biliary colouring matters after entering the small intestine.

(12) More minute chemical investigations of bilirubin and the other colouring matters of bile.

(13) General and precise information regarding the composition, constituents, and functions of the pancreatic, intestinal, and splenetic juices.

(14) The exact chemistry of excretine, excretolic acid, and stercorine (constituents of the fæces).

(15) The composition of the fæces in health and disease.

(16) A complete chemical investigation of liver-glycogen, and the ascertaining whether arterial blood can change it into sugar; if so, whether through the agency of any ferment whose existence depends upon the arterial condition of the blood.

(17) The chemistry of diabetes.

(18) The complete composition of lymph, chyle, and blood.

(19) Particular studies of the blood corpuscles.

(20) The chemistry of hematine, prepared by Wittich's process from hæmato-crystalline, with the view of determining whether it has definite connections with any of the colouring matters of bile or urine. This is not improbable as regards urine.

(21) A study of the action of oxygen gas upon serum of blood maintained at the body temperature, and also when artificially charged with food matters.

(22) The nature and general relations of the undetermined constituents of extract of meat.

(23) The colouring matters of the urine, taking up the researches at the points where left by former investigators.

(24) The composition of urine in disease.

(25) Further investigations regarding the chemical composition of the brain, directed particularly to ascertain the qualitative and quantitative differences presented by the white and grey matters.

(26) The elaboration of a quantitative method of analysis directed to brain matter.

(27) The chemistry of the so-called cerebrines.

(28) Further enquiries into the nature of the phosphorised principles of brain matter, with the view of determining the exact nature of certain unknown fatty acids, resembling biliary products, yielded in the decomposition of some of these, such as kephaline and the myelines.

(29) A better determination of the water extracts of brain matter.

(30) The chemistry of brain matter in all sorts of diseases.

(31) More exact information regarding the nature of the decomposition products resulting from the various albuminous substances of which different glands, tissues, and fluids are composed, or which they contain.

(32) Continued chemical investigations of pus, mucus, seminal fluid, milk, liquor amnii, &c.

(33) Studies to ascertain exactly by what chemical changes pepsin and peptones are produced from albuminous matters.

(34) The general chemistry of all albuminous matters, particularly as determined by the method used by Schützenberger, and by the method of hydration and limited oxidation combined.

(35) The chemistry of putrefaction, as compared with the results of the studies specified in number 34.

(36) The further study of the inter-relations between carbohydrates and fats.

(37) A precise chemical explanation of the Pettenkofer reaction. This would be best attempted, perhaps, by following up the steps described in Chapter XXIII.

(38) The chemical relations of choline or neurine to other similar ammonium bases, and their precise constitutions.

(39) Further investigations upon the phosphorised bodies referred to on p. 90 of this volume, and attempts to prepare amidated derivatives thereof, with the view of comparing the products to brain components.

(40) Prolonged studies of the physics of the body, directed particularly to work out the history of the force generated in blood oxidation.

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